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Foreword

MARTIN R. STEINBERG, M.D.

Most writers of forewords indicate how deeply flattered they are to have been asked. I would do the same except that it wouldn't be true. Instead of feeling flattered at being asked, I can say that I would have felt outraged if the request had gone to any other. As our careers have paralleled each other so closely, my being Director of the Hospital during the quarter century that Mo was Director of the Department of Psychiatry, it was quite natural, quite comme il faut, that I should provide whatever foreword is required for this volume.

I had planned to write at some length and to develop thoroughly the history of the Department and Institute of Psychiatry and to follow this with a scholarly, analytical appraisal of each Division, complete with personae and past achievements and future promise. That was until I saw the table of contents. Then I realized that, in the light of the full banquet that awaits you, all any reader would want from me at this point would be the merest aperitif. The Today and the Tomorrow of Psychiatry at Mount Sinai are brilliantly delineated in the pages that follow. I would like to dip, ever so briefly, into its past, although I am sure that this phase, also, will be covered in excellent fashion in Dr. Kolb's paper and others.

Before Mo's appointment as Attending Psychiatrist (which rapidly changed to full-time Chief of the Department of Psychiatry), the Psychiatric Service consisted of a psychiatrist who was a member of the Neurology Service. His role was to comply with requests from the other services for psychiatric consultations. Some such pattern was the common practice for practically all general hospitals at that time which, incidentally, was in the early forties.

In 1944, the Medical Staff and the Board of Trustees of The Mount Sinai Hospital jointly appointed a Special Committee to review contemporary currents in psychiatry nationwide, and to make recommendations concerning the future course of the Psychiatric Service at the hospital. This Special Committee, headed by Leo Gottlieb of the Board of Trustees, conducted a comprehensive study of existing patterns in psychiatric service throughout the land. They traveled to several of the major departments of psychiatry, listened to many experts, and pored over much of the current literature. Nearly a year after the Special Committee was appointed, it published its report, which contained the suggestion to establish what later became the Psychiatric Institute of The Mount Sinai Hospital, a Department that is larger in staff and scope of activities, I believe, than that of any other.

Let's go back half a century. In the Annual Report of the Hospital for the year 1920, Dr. Bernard Sachs, President of the Medical Board, reported: "A class for mental hygiene has been established in the Outpatient Department. In this class, advice and treatment are given to those presenting the earlier symptoms of mental states which, if disregarded, might later on lead to the development of more serious diseases of the mind. It is in this class that Psycho-analytic (sic) methods are pursued rationally and with very definite ends in view." In 1922, the Annual Report stated that "The Mental Hygiene Division has endeavored to popularize the Therapeutic Application of Psycho-analysis and has studied the problems presented by the various Psycho-neuroses." In 1924 the Medical Board reported, "The Mental Health Clinic has shown a distinct rise in activity. This Clinic treats patients suffering from mental disorders of a functional type. Three hundred and fifty new cases were admitted and often many hours have been devoted to the study of one patient."

During the Twenties, the Psychiatric Service at Sinai was beginning to grow and to make its presence felt. By the end of the decade, its members, writing from strength, had published papers on such topics as "The History of the Psycho-Analytic Movement in America" and "The Psychiatric Aspects of Drug Addiction."

By 1932, the Neurologica Service had an Associate Psychiatrist, three Adjunct Psychiatrists, eight Clinical Assistants in Psychiatry, and two Clinical Psychologists. A trickle of papers on "psychogenic" topics was beginning to flow from these psychiatrists based on their experiences in the Neurological Outpatient Service. In 1936, twenty-one such papers were published, ranging in topic from "Sigmund Freud: His Work and Influence" to "The Meaning of Childrens' Habits" and "The Psychological Study of an Hermaphrodite."

By 1939, the psychiatric staff had grown to 24, and the pattern of the future began to emerge. Says the Annual Report of that year, "The Psychiatric Division has been entirely reorganized during the past year. More expert psychiatric service is now available on the medical and some of the surgical wards, and in medical clinics of the Outpatient Department. The psychiatrists are now working shoulder to shoulder with the internists and surgeons and giving immeasurable assistance in the understanding and relief of many psychosomatic factors in disease. The reorganization of the Psychiatric Service constitutes an important change in the clinical services of the Hospital."

The following year, as the nation began to prepare for war, the department reported; "The Neuropsychiatric Service has been greatly enlarged during the past year. Four adjuncts in Psychiatry are providing psychiatric consultations to all services in the hospital. The Psychiatric Clinic has been greatly expanded so as to accommodate almost all applicants for treatment."

The same Report continues, "The Clinic, hard pressed for additional facilities needed to satisfy the demands made upon its services, introduced the so-called 'double-session days,' in which, instead of one group of physicians attending each morning, two groups attend—one from 9:00 A.M. to 10:30 A.M., and one from 10:30 A.M. to Noon. Thus, twice as many physicians can serve the Clinic . . . ." There were then 39 doctors on the Psychiatric Outpatient Service of the Neurology Department.

The combined Report for the years 1942/43, after noting simply that "the Mental Health Clinic was carried on with a depleted clinic staff," lists several departmental publications with unusually interesting titles: "The Organization of a Psychiatric Service for a General Hospital, "The German Cultural Paranoid Trend," and "Is Germany Incurable?"

The 1945 Annual Report of Mount Sinai is memorable on several counts. For the first time, it carries the listing "Martin R. Steinberg, M.D., Assistant Director." Also, this item appeared in President George Bernheim's Report: "Among the recommendations made by the Committee was one to establish Psychiatry in the Hospital as a separate Service equal to the other major Services. To head this newly established Service, the Board appointed Dr. M. Ralph Kaufman of Boston, who was recently in military service as Psychiatric Consultant in a major Pacific area," The same report refers, also for the first time, to what will be, seventeen years later, the magnificent Psychiatric Institute. President Bernheim's modest reference was as follows: "For the present, this new service will be rendered to patients in enlarged quarters in the Outpatient Department and on a ward presently vacant in the Medical Pavilion. *It is hoped to provide better facilities eventually in a new building for psychiatric patients* [Italics mine.]"

Enter Mo Kaufman. The Gottleib Committee was thorough. They wrought better than they knew. Long before they had ever heard of Mo Kaufman, they presented to the Board their specifications for the ideal man to head the new Department of Psychiatry. That these specs fit Mo and that he was located and that he was persuaded to merge his destiny with that of Mount Sinai is just one more instance of the hospital's legendary ability to attract the men Mount Sinai needs when it needs them. Let me share with you the Committee's recommendation:

> The Committee recommends that the head of the service should have the title of Attending Psychiatrist and should be a full-time paid man . . . . It will be the responsibility of the Attending Psychiatrist to organize, supervise, and develop the Psychiatric Service, including the Psychiatric Ward; the psychiatric investigation and treatment of patients in other wards, in conjunction with the parent Service; psychiatric consultations; the Outpatient Clinic (Psychiatric); the Division of Child Psychiatry; the teaching of the Attending Staff, residents, interns, nurses, and social workers; and clinical and laboratory research activities. The Committee believes that, while the Attending Psychiatrist must be a man of mature training, experience and judgment, he should be young enough in years to undertake the long-range development of the Service. In addition to first-class training and experience as a psychiatrist, he should be well grounded in internal medicine and neurology, although the Committee does not believe that he need necessarily be a qualified neurologist. The Committee believes that training in psychoanalysis would be most desirable, but not essential. If the Psychiatrist is analytically trained, he should not be of the type who considers analysis to be of such value and importance as to exclude all other forms of therapy. It is important that the Psychiatrist should be interested in, and have an aptitude for, teaching and research.

That was what the Committee wanted. What they got was M. Ralph Kaufman, M.D., C.M. Would that all Committees have their requests so amply granted.

Mo Kaufman had come to his true professional home and the pace began to quicken. He added both functions and staff as regularly as the years came and went. The Department of Psychiatry entered upon its cyclical pattern of development: Mo and his staff would recognize a need for a new or expanded service; they would begin providing that service with inadequate staff; he would then increase staff to fit the need. Then, the increased staff, operating from a larger base, would see new needs and new ways to serve the hospital, the patient and the community—and the cycle would start anew.

In the two dozen excellent articles that are comprised in this testimonial volume dedicated to Mo Kaufman, experts trace the growth and development of the many Divisions of the Department of Psychiatry under his leadership. There is no need to anticipate them here. However, if I might just dip briefly, here and there, into the Annual Reports of the past quarter century . . . .

In 1946, came the first (but definitely not the last!) of Mo's major reorganizations of the Department and the notice that, of his staff of 50, "a number of psychiatrists are working in liaison with other clinics, to help study the patients with reference to any psychiatric problems which may be presented." By 1950, this technique of providing liaison psychiatrists to all other services had proved so stunningly successful that a promising young administrator named Steinberg, writing for *The Modern Hospital*, reported, "In hundreds of ways, the liaison psychiatrist, by precept and by education, taught us to honor and to respect the entire personality of the patient, and taught us that so to dignify the patient would add much to the effectiveness of treatment, and would subtract many days from his necessary hospital stay. An important and valuable development that is beginning to flow from this service of the liaison psychiatrist—as a sort of extra dividend—is the subtle but definite and progressive change that is noticed, not only in the attitude of the nurses and other adjuncts toward the patient, but also in their attitude toward each other and toward the visitors and families of the patients. The process of dignifying the patient is wonderfully contagious. Apparently it becomes progressively easier to treat all of one's neighbors courteously once we dignify the one next door. While we have a long path to tread before we are satisfied with the level of courtesy and respect among all the employees, we cannot fail to notice that a momentum in the right direction has been achieved, and we are grateful indeed to our psychiatric service and its liaison psychiatrists for this large extra dividend."

If the practice of medicine at Mount Sinai had no more than this for which to be grateful to Mo Kaufman, it would still be greatly in his debt.

Child Guidance; Speech Clinic; Psychiatric Ward; Adult Outpatient Clinic; teaching seminars; Adolescent Clinic; research projects; cooperative training of Social Workers; Psychology Division; Follow-Up Treatment Clinic; Jack Martin Adolescent Unit; Residency training programs in adult and child psychiatry; Demonstration Unit for general hospitals everywhere—one after another, each came into being and each grew to become another formidable weapon in the assault on mental illness.

Along about 1950, Mo, in his annual departmental reports, began his soft-spoken but relentless crusade, "The Psychiatry Service generally showed continued progress, but may now be confined physically by the limitations of its facilities. Limitations of space make for unavoidable limitations of teaching and research programs." A similar plea accompanied each successive annual report until 1955 when the dream of an Institute of Psychiatry began to attain realization.

Then, in the President's Report for 1956, appear the exciting words, "I can now report that architects are working on plans for the building. It will occupy a site long held by the hospital on the west side of Madison Avenue, between 99th and 100th Streets. Two-thirds of the estimated costs are in hand." And, in 1959, the President reported, "The contract for the $16,500,000 nine-story building to house the Institute of Psychiatry was awarded to the lowest of nine bidders and ground was broken in August."

And, at long last, 1962 brought to Mo Kaufman the great reward for his equally great persistence and faith. From Mo's report: "For the Department of Psychiatry, 1962 was a year of momentous transition. The completion of the Esther and Joseph Klingenstein Clinical Center and the opening of our Institute of Psychiatry on December 18 represented the fulfillment of many years of careful planning and hard work. [Note: the formal dedication of the Clinical Center took place on November 14, 1962]. In anticipation of the Institute's opening, with an increase in capacity from 21 patients during any 24-hour period to 155 patients, a comprehensive reorganization of our department took place. Several new divisions were planned and a completely new table of organization was prepared to accommodate every aspect of the department's functions."

And, from the President's Report for the same year: "Our Institute of Psychiatry, occupying five floors of the Center, stands now as the largest psychiatric unit in any voluntary general hospital in the country, with the largest voluntary psychiatric staff of any general hospital."

As an amateur psychologist myself, I am impressed by Mo's application of Parkinson's Law, both before and after it was formulated. After years of wild growth—much like Alice after she took the bite of cake—until he was bursting the seams of the institution, it seemed that his every wish had been granted in the form of a five-floor institute large enough to accommodate all of the department's forced growth in prior years. And yet, his very first report after this magnificent new facility came into being speaks of "a comprehensive reorganization," "several new divisions," and "a completely new table of organization."

As this goes to press, Dr. M. Ralph Kaufman has 157 physicians and psychologists on the Attending Staff of his Department of Psychiatry. It encompasses the full panoply of psychiatric diagnosis, treatment, and research as the art and the science of Psychiatry have developed in this country. The department includes: Inpatient Services for Geriatric, Adult, Adolescent, and Child Patients; Outpatient Services for the same; the Day and Night Center; Somatotherapy Unit; Liaison Division, for both service and education; Research Division; 24-hour Emergency Service; Psychology Division; Therapeutic Activities Division; a school operated by the New York Board of Education; Community Service Division; Group Therapy Division; elaborate residency training programs; plus providing Faculty and courses for Mount Sinai School of Medicine.

Mo was one of the key group of Mount Sinai men who served as midwives for the birth of the School of Medicine. Primarily due to the work cum faith of just a few men like Mo Kaufman, the "impossible dream" of a great Mount Sinai School of Medicine became quite possible and now, of course, it is well on its way to becoming the standard by which proper schools of medicine will be judged. Naturally, Mo was asked to "double in brass" and to accept the deanship of the Page and William Black Post-Graduate School of Medicine of the medical school. In the 1969–70 academic year—the third year for the Post-Graduate School—more than 1,300 practicing physicians and dentists enrolled in 77 courses conducted by 133 Faculty members.

At the end of this volume, you will find an inspiring and yet sobering article outlining future goals for American Psychiatry by Dr. Roy R. Grinker, Director of the Psychiatry Institute of the University of Chicago's Pritzker School of Medicine. Roy was guest speaker at last year's annual Departmental Banquet and, without so much as a by-his-leave, I'd like to repeat here part of his heartfelt tribute to the subject of these pages.

> Twenty years is a short time indeed from its beginning in Ward A to its current status as one of the outstanding psychiatric facilities in the world. Within the walls of the Institute are conducted the most modern and varied methods of treatment; many innovations copied by other institutions (including my own); and an educational program for the Mental Health disciplines that is envied by all others—all of this could not have been developed without direction by an outstanding leader. Mo Kaufman readily demonstrates his grasp of every detail of our field, which has become a huge conglomerate of many activities. His energy and capacity for work are such as to exhaust me just by watching him. With all this, he has had time for the kind of scholarship hardly ever found in a professional. In addition, in his lifetime, he has spared no effort to contribute to our war effort and to city, state, and federal psychiatric affairs. I know you all love and respect Mo Kaufman, but I doubt whether you, within the house that he built, know the full extent of his positive reputation . . .

My personal feelings about Mo seem to be a blend of envy and pride—honest envy that I feel for a man whose all-absorbing life's work has turned out to be so grand and enduring a monument to his name as the Psychiatric Institute of The Mount Sinai Hospital; and pride that I was Director of the Hospital during the Kaufman years; that I was his professional colleague; and, especially, that Mo Kaufman was, and is, my very dear friend.

Mo Kaufman: An Appreciation

BERNARD C. MEYER, M.D.

Like the hero of Kipling's story, *How the Whale Got His Throat*, the protagonist of the present volume (which might properly bear the succinct title *How the Department of Psychiatry of The Mount Sinai Hospital Got Its Reputation*) could be characterized as a man-of-infinite-resource-and-sagacity. It is indeed in recognition of this felicitous attribute that these essays have been assembled, and, more particularly, it is to express some personal sentiments toward him that the present pages have been written. Mo belongs to that select company of persons—teachers mainly, friends sometimes—who, in the course of that serpentine path through which most of us have threaded our long and arduous way, are vividly recollected for the influence they have had on our lives or for the imprint they have left on our minds. Standing like directional highway markers, it is to them that we are inclined to ascribe the choice of the road we elected to take, no less than the origins and nurture of our taste, our style, and our values. As inheritors of the parental role—often at a time when the parents themselves are scorned—those few possess a potential for influence of which often enough they may be quite oblivious. (It is doubtful, for example, that a certain high school English teacher realized that what made Shakespeare palatable to a certain brash youth was the fact that this same teacher's Elizabethan scholarship had been supplemented by a most respectable career in semi-professional baseball, and that his precise knowledge of the exact text "All that glisters [not glitters, not glistens] is not gold," was matched by an equally precise knowledge of the exact definition of a pitcher's balk.) In the long parade of teachers, counselors, and so on that has passed before our eyes, such faces are rare, surviving in our memory like bright flags waving high above an army of gray shapes and monotonous sounds. For the physician that parade is virtually endless. Long after he has completed his formal medical training, his schooling continues, hopefully for the duration of his professional life; and at each successive step, if he is fortunate, there may be someone—an instructor, an intern, a resident, an attending member of a staff—who successfully has infused the dry dust of an anamnesis with the spirit of a living being, who possesses an unusual capacity for creating order and meaning out of an obscure and perplexing clinical picture, and who, finally, can transmit his own contagious compassion for human suffering to those about him. Given a position of leadership, such a man may exert a yet broader influence, for his enlarging reputation will attract others, irrespective of age or experience, and together they will create and foster a climate of learning and growth. Such indeed has been the influence of Mo Kaufman during the quarter of a century during which he has been Director of the Department of Psychiatry at The Mount Sinai Hospital.

As is true of many newcomers, his arrival late in 1945 was greeted with mixed emotions of which sentiments of cordial hospitality were probably the least conspicuous ingredient. As an intrusive outsider he was subjected to that thinly veiled suspicion and antagonism that is often accorded new arrivals in such private places as public conveyances and other already staked-out territories. Supporting this quasi-paranoid stance was the rumor that he intended to lay down a few ground rules for those good souls who were willing to work on his service. Only the momentum of his recent army experience, it was argued, could account for his temerity in demanding a minimum of six hours a week from the volunteer staff, and it was predicted that if, by any miscalculation, he should persist in his folly, he would soon find himself without any staff at all.

But these predictions failed to materialize, and although the six-hour requirement was not waived, the staff not only did not disappear, but grew from a handful of 17 or 18 in 1945 to 155 in 1970, which prodigious number has evoked no end of amazement and envy among our colleagues from other similar institutions. "How is it done?" they ask; and the answer they get is "Mo." For Mo is one of those exceptional beings, who combines within his person a triad of felicitous traits which, like the jackpot-winning combination of a slot machine, rarely appear together, but when they do give promise of a rich harvest and a cause for great rejoicing.

Mo is, to begin with, a clinician possessed of an unusually broad and profound knowledge and experience concerning the spectrum of psychiatric disorders and conditions, embracing not only the conventional neuroses and psychoses of everyday life but those occurring in times of war. His qualifications to establish a psychiatric service within a general hospital were further enhanced by his long-standing interest in the role of the psyche in physical illness and dysfunction. Of fundamental importance has been the fact that his approach to these and to many other clinical problems rests upon a basic and comprehensive training in psychoanalysis, the principles of which he has always regarded as the indispensible instrument for an understanding of any aspect of psychiatric phenomenology. For him to do otherwise would be as alien to his own scientific discipline as would be a musician's disregard of time and tonality or a bridge builder's indifference to elementary physics and to the dynamics of stress. It is indeed impressive to have observed Mo's faithful adherence to the fundamental principles of psychoanalysis while at the same time displaying the most elastic flexibility in exploring and testing new ideas in clinical psychiatry. As a consequence he is as attentive to the play of mental forces in the most "organic" of conditions, say, the psychosis accompanying disease of the brain, as in the most classical obsessional neurosis.

Second, he is endowed with a capacity to initiate and develop new ideas which, however bold and imaginative in conception, are at the same time susceptible to a practical implementation. Faced with the challenging and relatively novel assignment of setting up a psychiatric department in a large general hospital he saw the possibilities, not from the parochial point of view of establishing an enclave of mental patients, but rather, as a means of introducing and emphasizing the crucial interplay of mind and emotion in the general practice of medicine. It was not his intention, moreover, to restrict psychiatric consultations to dramatic emergencies, such as threatened suicide on the surgical service or an acute postpartum psychosis, but to establish a liaison service to the end that a psychiatrist would become an integral member of the staff of each nonpsychiatric department throughout the hospital, including outpatient facilities. The growth and development of this conception will be discussed in later pages; suffice it to say here that it has exerted a profound influence upon the climate of medical practice both at The Mount Sinai Hospital and in those institutions that have been modeled upon it. The nearly ubiquitous presence of a psychiatrist has served to focus attention upon such issues as the crucial interaction between psyche and soma, the placebo factor in all therapies, and the complex issues arising in the face of dying and death. It is hardly surprising, as will be emphasized later, that an impressive quantity and quality of original investigative work and publication has emerged from this program.

Yet nothing that has been accomplished within the past twenty-five years at Mount Sinai would have been possible were it not for Mo's remarkable capacity for leadership. It is this above all that has exerted a steady attraction upon an increasing number of colleagues, and it is this that has elicited from them an impressive manifestation of personal loyalty and of an eagerness to work together. For the past twenty-five years, for example, it has been the custom of our department to hold the so-called Liaison Conference every Thursday at noon. At some of these meetings the initial presentation of some extremely important psychiatric and psychophysiologic research has taken place, like Fisher's work on dreams and dreaming. Other maiden voyages launched at these meetings may have been either less virginal or less seaworthy, but in such matters one never knows in advance. One only knows that most of us will be there and that all of Mo will be. What is it in him that commands such spontaneous cooperation and devotion?

It is, I suspect, a number of things—his comprehensive scholarship, clinical acumen, and therapeutic optimism; his wit, his unabashed punning, and, despite adversity, his joie de vivre; his integrity, humanity, and other attributes of men of good will—but there is something more. It is notably the capacity to make an alive connection with another person and to make the other feel that he possesses a recognizable identity and an individual place and usefulness in the department. Mo has an unusual faculty for getting to know people and for remembering their names and for making himself accessible to them. Although he is a very busy person the door to his office is more often ajar than shut, and it is rather easy to open in any event. There, surrounded by hills of books and journals, which he succeeds in reading and digesting, he still has time to chat. Although it is natural that he has attracted some exceptionally gifted colleagues to the service, what is no less striking is his uncanny ability to find a place for some persons of seemingly limited talent and to extract from them an unexpected performance. As a consequence few members of the attending staff appear to suffer from that stateless sense of isolation that not infrequently afflicts the volunteer physician in many hospitals and clinics. He is no less hospitable to new ideas and has constantly encouraged their pursuit. He does not claim joint authorship for his colleagues' work, moreover; nor is he one of those chiefs who likes to see his name on every paper issuing from the department. His own lack of professional pettiness has filtered through the entire service to the end that he has established a harmonious family, endowed with a rare degree of camaraderie and amiability.

In a citation accompanying the awarding of the Bronze Star on February 4, 1944 to Col. Moses R. Kaufman "for meritorious service as consultant in psychiatry in the Pacific Theater," reference was made to his "initiative, tireless devotion to duty, and superior accomplishments." To us the language is familiar, for it anticipates in every detail the Mo we have come to know and love at Mount Sinai. For the many of us who have shared a good number of the past twenty-five years and for those who have been with him for a shorter time it has been both professionally and personally a memorable experience, a kind of golden age for which privilege we do not hesitate to thank this man-of-infinite-resource-and-sagacity. The present volume is our means of telling him so.

This appreciation, however, transcends Mo Kaufman's distinguished service at The Mount Sinai Hospital and embraces his example and his leadership as an influential figure in the sphere of American psychiatry. Not only in that sphere, but in our society in general, we are sorely in need of such leadership, for in both there are many who seem to have lost their bearings. We are living in an age when individualism threatens to be engulfed in a sea of anonymity, where the audacity of gangs masquerades as individual courage, where collective aimlessness is confused with personal freedom, and where a general disdain for craftsmanship and excellence is hailed as self-expression. The psychological implications of these trends are all too apparent—sensations are mistaken for sensibility, passionate interactions among the faceless participants of groups pass for meaningful expressions of human intimacy, private mental anguish is glibly ascribed to external malevolence, and the relief from inner torment is promised through insensate "crash programs" and the profligate and promiscuous expenditure of drugs and money. Though he shall receive no bronze star for it, Mo's refusal to surrender to such easy formulas is equally deserving of recognition. In the face of the noisy tempest of our times he has not mistaken an understanding of the mechanism of dreaming for an understanding of the stuff of dreams, nor has he confused the needs of a hungry body with the needs of a hungry heart. Consistent with the humanistic tradition and with the ideals of our profession, he has with unwavering insistence reaffirmed the truth of the poet's assertion that "the proper study of mankind is man."

When Jefferson arrived in Paris as representative of the government of the United States, someone is said to have commented, "Ah, you have come to replace Mr. Franklin." To which came the elegant reply, "No one can replace Mr. Franklin; I merely succeed him." A kindred sentiment is appropriate here. Although Mo will soon have a successor, neither his colleagues nor his friends believe that anyone will truly replace him.

M. Ralph Kaufman's Contribution to American Psychiatry

LAWRENCE C. KOLB, M.D.

To attempt to define a man's contribution to any profession or science in this century of rapidly expanding knowledge and technology requires a perspective of the vast changes that have taken place during this era.

M. Ralph Kaufman (Mo, to his friends and close associates) was born as the century opened, October 5, 1900. A glance at his professional curriculum establishes without any ambiguity both his insistent devotion to the study of man's mental suffering as expressed in abnormalities of thought, feeling, and behavior —psychopathology, as we call it—and his striving to understand and treat that suffering by mastery of the therapies evolving during the years, roughly, 1900–1970.

I came to know him first through the pages of the book *Teaching Psychotherapeutic Medicine*, edited by Geddes Smith, and published in 1947. It was in 1952 that I read his discussion of the physician–patient relationship—its many dimensions, pitfalls, and potentialities—interpreted so lucidly through the application of Freud's most significant contribution to our understanding of man's interactions with others, the transference relationship. That reading immediately imprinted Ralph Kaufman on my mind as an outstanding and masterly medical teacher. I looked forward to meeting him. When that occasion occurred within a few years, my expectations were upheld. But more of that later.

To define Mo Kaufman's contribution we need some general record of the evolving role of psychiatry, psychoanalysis, and the other biosocial sciences over the span of his lifetime. So, too, we should place on record the differing ways men were trained to practice this specialty, the changing interests they pursued in their professional growth, and the forces which induced those changes.

At the turn of the century there were few physicians who would have predicted the great development of psychiatry as a specialty. To be sure, the increasing burden of care of the hospitalized mentally ill had become apparent both to those in government charged with the financing of health care and to the few physicians who were moved by some humanitarian concern to offer treatment or who felt challenged to undertake a study of the etiology of the mental diseases. In 1900 the physician interested in mental diseases was found, for the most part, attached to the isolated public mental hospitals, the few private institutions, the city receiving wards, or in private neurologic practice. His therapeutic armamentarium was meager. It consisted principally of his own personality and an intuitive understanding of others, and, secondly, of a judicious use of moral suasion or admonition, of narcotics and sedatives, and the prescribing of regimens of bathing, rest or work, exercise or travel.

His task, as far as instruction of medical students was concerned, even in the oldest and best organized colleges of medicine, consisted of two or three clinical demonstrations of grossly disturbed and pathetically psychotic patients—a sterilized version of a Sunday's walk through London's Bedlam of previous centuries. This usually was the extent of the medical students' exposure to psychiatry—an exposure which probably did more to deter his interest and to instill in him the same anxious abhorrence and frightened avoidance of the sufferers of these illnesses that so widely pervaded the public at large. Indeed, that frightened avoidance and the shame attached to mental illness were widespread and profoundly felt. Although they may have been attenuated somewhat in the past quarter century as we have come to understand the biological, psychological, and social forces that determine for the sufferer the development of these illnesses of mankind, they are still with us. Even today, one cannot arouse widespread public interest in philanthropic efforts to educate or initiate research in this area of medicine. Only those who have had within themselves the courage to examine the frailties of the human mind, to comprehend the intensity of pathos in its suffering, and the humanity to wish for its relief, practiced and encouraged private and public support to advance the growing need for the cure of the mentally ill.

As one looks back to the turn of the century, it is possible to discover that there existed even then the thoughts and efforts and beginnings of new knowledge upon which rest the roles and functions of modern departments of psychiatry. There was a mounting interest in studying brain structure and function and an attempt to correlate these findings with abnormalities of mental functioning. But also there was emergent an effort to clarify human behavior, particularly its pathologic expressions. The validity of psychic causation became convincing through study of hypnotic phenomena. The beginnings of psychoanalysis posited dynamic explanations for the occurrence of neurotic symptoms. Those same studies revealed the necessity of concentrating on the developmental experiences of the infant and child within the context of his family in order to understand the evolution of those patterns of behavior which characterized his later personality. Just before the turn of the century in New York, the state established a multidisciplinary research institute that gave recognition to the complexity of the determinants of mental diseases by making appointments of scientists in the fields of anthropology, psychology, and cellular biology, as well as in pathology, bacteriology and medicine. It was apparent then that the emerging specialty of psychiatry, no less than general medicine, required an alliance and collaboration with the biological sciences, as well as with those psychosocial sciences now so widely recognized as sources of potential information on the causes or processes of determining pathologic behavior.

Psychoanalysis came to the United States in the first decade of the century, and the knowledge of its theory and application of its practice steadily grew thereafter. But the skill of its practitioners during World War II in the treatment of the many stress reactions of that period was responsible for the greatest and most eager rush of new aspirants to the psychoanalytic institutes since the turn of the century.

So, too, the empiric discovery of the effect of the shock therapies in modifying symptom expression and the development of psychosurgery in the 1930's continued to stimulate interest in study of brain function as related to behavior. These methods of therapy and related areas of inquiry were supplemented after 1950 by the use of new pharmaceuticals, particularly the phenothiazines and the antidepressants. Their introduction also opened up new lines of biochemical investigation from which have emerged powerful models for explanation of transmission of nervous impulses in the brain. Clinicians, comparative psychologists, and ethologists have amassed a vast array of observations concerning the impairing effects of deprivations in early life upon later development. And, too, there emerged studies of the physiology of sleep and dreaming and of certain behavioral consequences of disturbance of these fundamental physiologic processes.

At the same time, a broader application of humanistic trends in the operation of mental hospitals and a recognition of the supportive or destructive social interactions in the therapeutic environment have revolutionized the care of the mentally ill. There has arisen a new comprehension of the therapeutic roles of the modern psychiatric nurse, social worker, and activity therapist within the framework of a sociotherapy which makes active contribution to ego development or maintenance. With new understandings, the cultural variants of behavior, both adaptive and maladaptive, have become increasingly appreciated and recognized.

With the progressively successful conquest of infectious illnesses and the control of a host of other metabolic, degenerative, and neoplastic conditions during the second quarter of the century, the public expectations of the curative powers of physicians expanded immeasurably. There now flock to clinics and doctors' offices an increasing number of individuals whose troubles are expressed in terms of social disease alone or whose physical symptoms derive from or are aggravated by social disease. However, the rapidly expanding theoretical and factual knowledge upon which rest the impressive clinical advances of contemporary medicine has claimed increasing time and attention in the curriculum of the modern school. As a consequence, some clinical instructors make it appear that they can ill afford to invest time for the teaching of the art of medicine—notably, the human contact of physician with his patient, the demonstration of the intuitive comprehension of the emotional state of the sick person, and the interpersonal response best suited to alleviate the latter's disrupting fears and anxieties. Many believe it is this loss that has led some segments of the public to express dissatisfaction with their personal contacts with physicians. One might conclude that, as a consequence of the technological and mechanistic successes and the attendant changes which modern medicine has achieved, the departments of psychiatry with their humanistic tradition arose as a necessity.

Certainly the central role of the department of psychiatry in the faculties of medicine is the teaching of all that is now pertinent to the understanding of disturbed behavior and thought in man, the means for its diagnosis and evaluation, the measures for its alleviation or surcease, and their indications and risks. Within the circumscription of that role there exist those others which bring to each faculty and its student body a continuing sense of awareness of human relations, their evolution through family and cultural transactions over time, and, even more important for every practitioner of medicine, a theory of practice and interpersonal relations which defines the particular nature of the therapeutic bond between patient and physician.

Thus, the fields to which the major actions of psychiatrists have committed themselves have shifted immensely over the half century of Dr. Kaufman's professional years. In the nineteen twenties there were only the beginnings of university clinics and general hospital units accepting and treating the psychiatrically ill. For the most part the latter were cared for in specialized psychiatric receiving hospitals in large metropolitan areas such as, the Bellevue unit in New York, or the Cook County Hospital unit in Chicago. In Baltimore Johns Hopkins had its private Henry Phipps Psychiatric Clinic. Elsewhere medical students and physicians aspiring to become psychiatrists trained in the state and private psychiatric hospitals or special institutes such as, the Boston Psychopathic Hospital, the New York State Psychiatric Institute, and the Michigan Neuropsychiatric Institute. The private practice of psychiatry and psychoanalysis was limited.

All this was to change. Today the most active centers of hospital practice of psychiatry exist in the general hospitals. Almost five hundred services of psychiatry, including inpatient services, operate in the general hospitals of the United States of America. Annually, the first admissions to these inpatient psychiatric services of the general hospitals exceed those to the state psychiatric hospitals. In an age of enthusiastic discussion over community mental health and the need for decentralized services through establishment of community mental health services, the widespread, highly successful, and already existing network of general hospital psychiatric services go about their daily service largely unrecognized and unsung. And it is to the general hospitals that the seriously ill traditionally beat their way, as they have for centuries. What is genuinely new and creative in the past quarter century has been the acceptance and development of the psychiatric services in the general hospitals of the country. This imaginative development within the traditional framework of delivery of health services called for a major effort in public and professional education directed to removing the walls of shameful anxiety and despair that isolated the mentally ill from the primary centers of health care.

But the advances in the general field of medicine during the last half century have brought new problems to the interface between medicine and psychiatry. Particularly as the future opens to control population growth through acceptance of chemical agents or abortion for birth control and for organ transplantation to rescue many from hitherto helpless illness, a host of ethical, moral, social, and individual conflicts are generated. Today a greater hope for the prolongation of life for the individual is in conflict with the threats of an overwhelming population explosion. Despite attempts to define by scientific means those brain functions which are consistent with human life, the issue of organ transplant continues to present a vexing moral issue for it devolves upon the right of the individual for biological existence above and beyond the difference between human life and death. Hopefully, this question will be solved through long and intensive social conflict and questioning. As that goes forward, psychiatrists in our hospitals will be increasingly called upon to protect and heal their fellow men torn by those heartrending decisions as they seek continued life for a loved one through accepting the offer of medicine's technological brilliance, or when they are requested to give the biological life of their loved one to someone else.

In this kaleidoscopic sketch of change of the past half century Mo has carried on his professional life, giving completely of himself to the repeated challenges which have confronted him as a physician, psychiatrist, psychoanalyst, and educator. Through the chance of his birth, he is blessed with exceptional intellectual endowment, a personal family life in three different countries, and a most unusual sequence of educational experiences. These have been times that demanded men of broad culture with compassionate understanding of the struggles and trials of many other men. So, too, as always, they required high energy and intensive dedication to the goals to be achieved. As a modern educator one needed, too, intellectual talent well honed through academic pursuits, curiosity about the little known or unknown, coupled with the personal freedom to allow and support exploration, to stand for and work for change when the tested new discoveries promised help for others. Mo has all these qualities. He has others, as well. Not only does he strive for excellence in himself, he respects and expects similar efforts in others. When convinced of the inherent propriety of some policy, some attitude or experience in fostering excellence, his is an impassioned defense of that position, given with an insistent, well turned, and often vehement expression. But, too, he can turn from the serious to become a delighted expositor of the ribald story. He is a gifted storyteller endowed with an ability to withhold the punch line to precisely the right moment. There are few who have a fund of stories to match his, stories which spare neither himself nor his profession. Perhaps beyond all else is the satisfaction he receives in his relationships with his colleagues, his students, and with his family. He possesses a special gift for conveying to others his immense gratification in scholarship, in probing the unknown, in challenging cant or the sensational, and in clarifying the significant lines of thought.

How did he acquire these traits which all of us have come to love, respect, and admire? Born in Beltz, Bessarabia, Russia, on October 5, 1900, young Moses came to Canada with his widowed mother at the age of five. Mo has two brothers and one sister, all living in Canada. Following his primary and secondary schooling, he attended the McGill University Medical School, Montreal, where he received the degrees of M.D., C.M. in 1925. (His brother, Dr. Manuel Straker, now holds a faculty appointment as Professor of Psychiatry in this same school.) It was his mother's long struggle in raising her family, coupled with his interest in history and the law which seemed to have laid the foundation for his interest in the human condition and in psychiatry in particular. Young Dr. Kaufman moved to the United States immediately after receiving his degree to serve an internship at the Manhattan State Hospital. There his educational program was influenced by Dr. George Kirby, the Director, who later came to direct the New York State Psychiatric Institute. He was also influenced by the eminent neuropathologist, Dr. George Dunlap. (It was there that he met A. A. Brill and Phillip Lehrman, who were consultants to the hospital.) As part of the experience, he served as well in the Vanderbilt Clinic prior to its move to the then newly built Columbia-Presbyterian Medical Center. Dr. Kaufman next elected to study neurology and spent the academic years 1926–1927 at the Montefiore Hospital in New York City where he came into contact with that brilliant group of neurologists—Drs. Israel Wechsler, Moses Keschner, S. Philip Goodhart, Isadore Abrahamson, and Samuel Brock.

His future course was fixed with his next move. Appointed an assistant at the Boston Psychopathic Hospital, then under the leadership of C. MacFie Campbell, his talents as a psychiatrist came to quick recognition. He was awarded an appointment as a Commonwealth Fund Research Fellow of that Hospital and the Harvard University Medical School. He held that appointment for the succeeding three years. During this same period, he spent sixteen months at the University of Vienna in the Anatomy and Psychiatric Institutes. It was here that he began his psychoanalytic training in the Vienna Psychoanalytic Institute. His personal analysis was started with Dr. Paul Schilder and finished under Dr. Wilhelm Reich. On his return to the United States, he became a member of the New York Psychoanalytic Institute in 1932.

The broad outline of his postgraduate education was complete—neurology, psychiatry, and psychoanalysis. His "Wanderjähre" brought him both a new understanding of psychoanalysis, as well as an appreciation of the research potential of the biological sciences as related to brain functioning and personality.

In these years Dr. Kaufman's name appeared first in the professional journals as the author of various papers written from his observations and reflections concerning clinical conditions and pharmacological substances influencing behavior. As might be expected, the initial papers were concerned with neurological disease. The first concerned dystonia; the second, the fascinating drug, bulbocapnine, as related to dyskinesic illness. Those others which followed quickly reflected his shift in interest to clinical psychiatry. In 1929, he coauthored with Jacob Kasanin a monograph entitled *A Study of the Functional Psychosis in Childhood,* which was based on extensive clinical research and was an important early contribution in this area. A number of papers reported his experiences with psychoanalytic therapy in schizophrenia, as well as late-life depressions, and the use of carbon dioxide and intravenous sodium amytal as therapeutic agents in psychosis. By 1932 his clinical contributions dealt with psychopathology, its dynamic explanations, and a beginning preoccupation with psychosomatic relations. As an expositor of facts and ideas he has become an associate editor of the *Archives of General Psychiatry* and the *Psychiatric Quarterly,* as well as Contributing Editor to the *Israel Annals of Psychiatry and Related Disciplines* and *Medical Insight.*

His return to Boston as Clinical Director of the distinguished McLean Hospital filled out his clinical experience. It was between 1933 and 1945, while serving as attending neuropsychiatrist at Boston's Beth Israel Hospital, that he laid the firm groundwork for the practice of psychiatry in a general hospital. Here he had the opportunity of reorganizing the psychiatry service. His attendance there must have etched out for him the salient clinical problems of psychiatry in the general hospital, highlighted the abilities and the limitations of his medical colleagues in the management of patients with emotional reactions, and outlined the areas appropriate for psychiatric research. This was the very groundwork that ensured his aptitude in the position of leadership he was to fill at The Mount Sinai Hospital in New York.

In the psychoanalytic field these years, too, were active ones for Mo. He became a member of the beginning Boston Psychoanalytic Society in 1930. Drs. Ives Hendrick, Leolia Dalrymple, John Murray, and Mo came together in the Freud Seminar—the beginning of organized training programs in psychoanalysis in Boston. Their teachers there were the younger members of the Educational Committee of the New York Psychoanalytic Institute: Drs. Bertram Lewin, Dorian Feigenbaum, Abram Kardiner, and Gregory Zilboorg. In March of 1931 he presented a paper on the work of Wilhelm Reich before the Society and later undertook a control analysis with Dr. Franz Alexander in addition to working with Zilboorg and Bert Lewin. The development of the Educational Committee of that society, that is, the progenitor of the Boston Psychoanalytic Society, took place during these years. Dr. Kaufman was a participant in this step in psychoanalytic evolution. His experience in the Boston Psychoanalytic Society led to the drafting, with Dr. Richard Frank, of an important resolution accepted by the American Psychoanalytic Institute in 1951 which established clearly that the education of psychoanalysts acceptable to that national body was a function of the Psychoanalytic Institutes and not of individual psychoanalysts. In his lively monograph *The Birth of an Institute* (Bond Wheelwright Company, Freeport, Maine, 1961), Ives Hendrick has recorded the spirited discussions and decided points of view that characterized the positions which Dr. Kaufman and others took in the beginnings of formal psychoanalytic education in Boston.

The war years did not interrupt his active clinical teaching. Dr. Kaufman volunteered for service and was activated in June of 1942. He developed plans with Lt. Col. Malcolm Farrell and Col. Roy Halloran for the Army School of Psychiatry while serving at Walter Reed General Hospital in Washington, D.C. Ten months later he became an Executive Officer of this school at the Lawson General Hospital. But service within the continental limits of the United States was not to be the extent of his war experiences. He was assigned to the South Pacific (USAFISPA) as Consultant to Neuropsychiatry. As neuropsychiatric consultant he served in the South Pacific, then the Pacific Ocean Areas, and later the Sixth Army in the Philippines.

During this period as consultant he participated actively in five campaigns. This presented him with an opportunity to participate in all phases of the medical planning for these campaigns and to work out programs for all aspects of psychiatry in combat. He was able to work effectively with the Command

Headquarters which resulted in a well integrated psychiatric program which was related to all medical aspects in the theaters. The departments of psychiatry from the station to general hospital were organized as dynamic, diagnostic treatment centers. Under combat conditions, psychiatry was able to demonstrate its therapeutic effectiveness, particularly in the Okinawa Campaign. A dramatic account of front-line psychiatric rehabilitation was written by a war correspondent for *Collier's*, in which Lieutenant Colonel Kaufman and Maj. Lindsay Beaton were described treating and restoring men to the front lines by immediate psychotherapeutic and hypnotic treatment.

His special dedication and efforts were rewarded by five Campaign Stars, the Bronze Star Medal, and the Bronze Star Medal with Oak Leaf Cluster for his active participation during these campaigns. In addition, there were a number of commendations from Commanding Officers of various units within which he had set up active psychiatric programs. On December 23, 1945 he was promoted to the rank of Colonel, shortly to leave the service for a most important responsibility in New York City. Most of his contemporaries who gave of themselves to the armed services of our country during World War II learned much working with others and learned, too, by that experience, of the organizational measures which might be used to insure effective working relations within groups. While Mo already had some experiences of this kind before his service in the Army of the United States, undoubtedly he gained more insight into the problems of leadership and administration while serving his country. He remains sincerely and deeply proud of his service to his adopted country. The experience he gained in service he would later need.

Those responsible for implementing and maintaining high levels of clinical practice at The Mount Sinai Hospital in New York recognized his unusual talents, training, and experience. In their desire to establish a preeminent department of psychiatry in this outstanding general hospital, they convinced him to become the first full-time director of the service, a post he assumed in 1945. So, too, the faculty of the Columbia University College of Physicians and Surgeons was equally perceptive and appointed him as Clinical Professor in the Department of Psychiatry. My coming to the college brought us closely together for the first time.

The impressive story of the growth and development of the psychiatric service at Mount Sinai over the past 25 years with its great contribution to patients, the education of general house officers, young psychiatrists, and other mental health professionals, as well as to research, fill the later pages of this volume. The new chief served as a model to others. He attracted able staff and young physicians aspiring to become psychiatrists. His erudition and scholarly interests were evident in the continuing stream of published writings on topics concerned with psychosomatic medicine, psychotherapy, psychoanalysis, psychiatric education, and history. With the founding of the Mount Sinai School of Medicine in 1964, he was appointed Professor and Chairman of the Department of Psychiatry, and later invested with the endowed Esther and Joseph Klingenstein Professorship in that department. He aided the development of the new medical school in whose founding he played such an important role by agreeing to serve, as well, as the Dean of the Page and William Black Post-Graduate School of Medicine. Meanwhile he continued to be Psychiatrist-in-Chief to the hospital. But Mo's activities have not been restricted to the Mount Sinai community. Shortly after the conclusion of World War II he participated actively in the formation of the Group for the Advancement of Psychiatry. He was a "charter" member for 10 years of the American Medical Association Mental Health Council. He was active on the Joint Commission on Mental Illness and Health, and functioned as Chairman of the Committee on Studies. His high standards and dedication to education placed him in 1964 as a member of the Residency Review Committee of the Council on Medical Education and Hospitals of the American Medical Association; he has been a member and, later, Chairman of the Council on Medical Education and Career Development of the American Psychiatric Association; and a member of the Training Committee of the National Institute of Mental Health.

His professional colleagues elected him to be President of the American Psychoanalytic Association in 1949–1951, and as Council member and later as Vice-President of the American Psychiatric Association (1963 64). He served as Vice-President of the New York Academy of Medicine from 1960–62. He has been a member and Chairman (1965–68) of the later Committee on Medical Education, as well as Chairman of the Medical Advisory Board of the Hebrew University, Hadassah Medical School, Jerusalem, since 1961. His numerous memberships in other scientific societies and social clubs demonstrate the extent of his great interest in the work and society of his fellows.

American psychiatry and psychoanalysis is deeply indebted to M. Ralph Kaufman as his efforts fostered the development and expansion of psychoanalysis in this country, its acceptance into the body of psychiatric theory, and its important application in the field of psychosomatic medicine. The general hospital service he developed at The Mount Sinai Hospital in New York has served as a model for the evolution of general hospital psychiatry at its best. His contributions to the educational scene, to setting high academic standards and values are enormous. Also noteworthy is the support and encouragement he has provided to some of the most significant investigations of the past several decades, particularly as related to the physiology of sleep, to the problems of alimentary dysfunction, and to other avenues to new understandings of the mind–body relationship.

Nor have these contributions existed at the expense of his personal life. Mo is a wonderful family man, a devoted husband. Married to Ida Elizabeth Esach on September 2, 1925, they have been blessed with a daughter and son, both now married, Bettina Deborah Kahn, and Paul, now an Associate Professor of Psychiatry at the Boston University Medical School.

Many of us have enjoyed the friendship and warm hospitality of the Kaufman family. We owe them a great debt for their commitment to human life at its best, and so we honor them in this volume dedicated to M. Ralph Kaufman, a man of courage, of untiring and energetic drive toward his goals, and of constant dedication to the service of others.

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The Psychiatric Inpatient Service

EDWARD D. JOSEPH, M.D.

From the inauguration of the Psychiatric Inpatient Service of The Mount Sinai Hospital in February, 1947, to the present day, two guiding principles have prevailed. Of these, the first asserts that psychiatry is a component of the science of medicine and, as such, has the potential of making important and often vital contributions to an understanding of the genesis and treatment of a wide variety of disorders. In keeping with this principle, it has been the policy of the Department of Psychiatry at The Mount Sinai Hospital to demand that a psychiatrist working on the service be a man well versed in medicine, familiar with the physiological functioning of the body, and aware of the potential impact of those functions on mental activity as well as the converse. He need not be a specialist in a variety of somatic conditions as much as an alert clinician mindful of their common interactions with psychological forces.

The second principle states that a psychiatry service in a general hospital should achieve three essential goals: rendering service, providing training, and encouraging research.

The initial inpatient facility was a 22-bed ward (known as Ward A) which was located in a formerly unused, but much traversed, portion of the old hospital building. Ward A consisted of a large 10-bed room, in which the only partitions or separations between the beds were hanging curtains. The other 12 beds were located in two-bed and four-bed rooms adjacent to a dark corridor. The office of the chief resident was located directly on the 10-bed ward, which also contained a glass-enclosed nurses' station. The kitchen and utility rooms were adjacent to the various side rooms utilized for patients. A very small patients' lounge was located next to the large ward, as were offices for the other residents and for the chief social worker. Not far away were the offices of the director of the department and of the chief social worker. Thus the unit as a whole was compact, with everyone having easy access to everyone else. Both male and female patients were admitted to Ward A, but they had separate sleeping accommodations. The two- and four-bed rooms were utilized for either male or female patients. The ten-bed ward served as a female dormitory almost exclusively throughout the history of Ward A. The lounge, of course, served for all patients.

It was assumed from the beginning that these facilities were only temporary and that eventually there would be an institute of psychiatry in the hospital. This "temporary" phase lasted from the opening of the ward in February of 1947, to the beginning of 1962, when the Psychiatric Institute opened as part of the Klingenstein Clinical Center.

Although the capacity of Ward A was listed as 22 patients, it was the usual practice to have from 18 to 20 patients at a given time, with several beds reserved for emergency purposes. At times, of course, the census exceeded the official capacity; additional space was then provided, either in the two-bed rooms or, on some occasions, by placing a bed in the chief resident's office, the door of which had been made wide enough for just such a purpose. In this way too, a critically ill patient could be separated from the remainder of the ward population.

In the beginning it was decided that because of the limited capacity of the ward, it would not be possible to provide general psychiatric service to the community; instead, service would be provided only for those psychiatric patients within the hospital community whose physical condition necessitated hospitalization. This concept of a psychosomatic service caused the ward to be occupied by individuals suffering from a variety of physical conditions—such as, asthma, peptic ulcer, ulcerative colitis, various skin conditions, lupus erythematosis, rheumatoid arthritis, obesity, anorexia nervosa—and other physical conditions in which a psychological factor is believed to play a predominant role. As a result, there were often patients who were extremely sick both physically and psychologically.

Staffing patterns on the service reflected both the philosophy of the department and the needs of the patients. The psychiatric residency staff was supplemented by an assistant resident in medicine who spent three months of his rotation on the "psychosomatic" service. Furthermore, in addition to the attending psychiatrists who supervised the work being done on the service, there were always one or two liaison internists assigned by the Department of Medicine to supervise the medical care of the physically ill patients on the psychiatric service. This staffing pattern has remained essentially unchanged in principle ever since, although it has increased in number both at the resident and attending level. However, at present, interns from the Department of Medicine, rather than assistant residents, rotate through the psychiatric service, and the number of liaison internists have increased as the service has expanded.

The training aspects of the inpatient service were planned for from the very beginning. The work of the residents was supervised at first by two attending psychiatrists (Drs. Harry Weinstock and Abram Blau), one of whom came in early in the morning, the other early in the afternoon; they were available, moreover, for any untoward happening. In addition, the medical liaison man attended daily. Conferences and ward rounds were conducted by the attendings every day. The residents participated in a formal case presentation with Dr. Kaufman, whose advice and counsel were readily available and unusually informed because of his keen interest in the inpatient service. In addition, other informal supervisions were provided by various attendings who were interested either in specific patients or specific problems. Over the course of the years the inpatient service and its resident training program were supervised by attendings of high-level training and experience. Service on the ward has always been regarded among the attending staff as a choice assignment, providing both challenging patient problems and teaching opportunities.

There was a staff of six to eight nurses available for the ward service under the leadership of a charge nurse who was an experienced and capable individual, knowledgeable both in medical and in psychiatric nursing. As the psychiatric inpatient service expanded and gained experience and knowledge, a number of student nurses received their psychiatric training there. After they had been graduated many of the nurses came back to work on our service.

The social service department headed by Miss Frances Spiegel was an integral component of the work on the inpatient service from its inception. Miss Spiegel's office, adjacent to the ward, made her readily available for information and counsel, and innumerable miscellaneous favors which she supplied so graciously. She gradually took over many administrative functions as well. In addition to her, there were various social workers assigned to the service who became invaluable members of the therapeutic team.

The psychological services were provided by Dr. Fred Brown and his staff. In the early days of the service every patient was seen by a psychologist, whose reports were of great assistance in arriving at a diagnosis and in planning a treatment program. We still strive to refer every patient to the psychologist, whose report is viewed as an integral part of the total clinical study.

There was evolved a team approach to the treatment of patients made up of the combined efforts of doctors, nurses, social workers, psychologists, and other personnel.

For most of the time that Ward A existed, it was possible for patients to be kept in the hospital as long as their condition, either physical or psychological, indicated. Thus it was not uncommon to have patients with ulcerative colitis, for instance, stay on the ward for periods up to 6 months or so, while others with more rapidly responsive conditions would stay for shorter periods of time. All patients were "service" patients (i.e., non-private) and were treated by the resident staff.

The prime modality of psychological treatment was individual psychotherapy performed by both psychiatric and medical residents. It was the intention, usually carried out, that each patient would be seen daily by his resident in an individual psychotherapy session. It was made abundantly clear to the residents at the outset that there was a profound difference between psychoanalysis and psychotherapy and that they were practicing the latter. The attendings were, by and large, all psychoanalytically trained and oriented, while the residents had not been psychoanalytically trained. However, they were taught psychoanalytic principles and the application of these to dynamic psychotherapy. As the service evolved, the attendings and residents became aware that patients interacted with one another. Advantage was taken of this to introduce modified forms of group therapy.

As the years passed, other changes began to take place in the therapeutic approach to patients. In addition to the psychotherapy done by the residents on the ward as part of a total treatment team, an expanded social service staff undertook work with the family and with the environment to which the patients would ultimately return. To help patients with their recovery from their psychophysiologic illness, rehabilitation efforts were undertaken, and the beginnings of occupational therapy and rehabilitative therapy were started.

Gradually, with the knowledge that a psychiatric institute would be provided and available in a new building, plans were made to change the nature of the inpatient service population in accord with the anticipated expanded facilities. The patient population began to shift from those psychosomatic disorders for which the patient had often initially been admitted elsewhere in the hospital, to conditions that were more primarily psychiatric. This allowed for a larger number of direct admissions from the community, paving the way for the expanded service that came into being in 1962 with the completion and opening of the wards in the Klingenstein Clinical Center.

Along with this expansion came preparation for the use of more attending psychiatrists on the inpatient service. The nursing service, social service, psychological services, and occupational therapy were also similarly prepared for the anticipated expansion. The assignment to each unit of a chief resident and three assistant residents, aided at times by fellows in training, for varying periods of time served as the staffing pattern for the new service when it expanded from a single 22-bed ward to four 22-bed units. In addition, the new inpatient service provided for a ward for possible use by the children's service, a facility that had previously been lacking. Finally, a sixth ward was set up as a day and night center utilizing newer concepts of inpatient facilities in a general hospital.

Thus in 1962 when the Klingenstein Clinical Center opened it was possible to have four adult wards for inpatients, a children's ward accommodating 15 patients, and a day and night center accommodating approximately 20 in the night center and up to 40 in the day center. All of the expanded staff for such an increased undertaking had been planned for, and was rapidly assembled as the facilities came into being and into use. With the enlarged facilities and resident staff, an expanded residency training program was put into effect, allowing for the training of some 36 residents in the adult service and up to seven or eight in the children's. A supervisor of nurses for the entire psychiatric service was appointed, and assignments were made for chief nurse and appropriate other nurses for each unit. Ample space was provided for occupational therapy and a department of recreational therapy. The expanded social service department provided for a supervisor of psychiatric social workers, and for at least one social worker per unit, both child and adult. An analogous expansion occurred in the Department of Psychology.

As noted above, with the marked expansion of facilities came a complete change in the nature of the patient population. This change was brought about by a combination of factors, including the development of new treatments for psychophysiologic disorders, the growing recognition in the general community of the desirability of earlier hospitalization for psychiatric patients, and the need of the inpatient service for an adequate number of psychiatric patients to continue the training and research programs that had been started. As a result, patients were admitted more directly to the psychiatric service from the community at large and represented the gamut of psychiatric disorders. Highest priority for admission at present has continued to be given to those patients hospitalized elsewhere in the Mount Sinai complex, requiring psychiatric treatment in the course of their period of hospitalization. Along with the expansion of facilities and the size of the attending staff (now numbering about 155) many more psychiatrists became involved with the inpatient service as supervisors and as teachers. These attendings were given the privilege of hospitalizing patients, a move which for some meant some alteration in their previously existing clinical practice. Many began to treat more acute patients whom they could hospitalize and follow during their hospitalization.

An additional factor playing a role in the change in the hospital population consisted in new treatment methods that were introduced as rapidly as they became available. Whereas in the early days of the inpatient service electroshock was not administered, it was introduced as a treatment modality in the early 1950's, and has remained an integral part of the therapeutic armamentarium since that time. A special electroconvulsive therapy unit was set up under the guidance of a trained attending psychiatrist. In the early 1960's came the introduction of more specific psychotropic drugs such as the phenothiazines for schizophrenia and marked anxiety states and anti-depressive drugs of greater specific action than those existing before. While the cornerstone of treatment has continued to be individual psychotherapy performed by residents under the close scrutiny and guidance of highly trained psychiatrists, there has been a growing tendency for use of the various psychotropic drugs.

The change from the beginning of the inpatient service to the present day is best illustrated by a comparison between the experience of the first two years of the inpatient service, and by a survey of what has occurred within the past year. In the first two years of the inpatient service there were no specific psychotropic drugs used, and even such drugs as sedatives were used sparingly. In the past year a survey shows that sedation was used frequently. Specific psychotropic drugs were ordered on almost 95 percent of all patients, as indicated by the results and spot checks on three different occasions during the year. This use of drugs in addition to psychotherapy occurred both for the adult patients and on the child service.

To maintain the quality of work of the residents in their psychotherapy, each unit is headed by a senior attending psychiatrist assisted by a staff psychiatrist (usually a recently graduated resident psychiatrist), who is involved in the actual training and education of the residents. In addition, each unit is assigned a certain number of preceptors—psychiatrists of senior status and training—to supervise the individual therapy and management of their patients.

Other treatment modalities have also been introduced or elaborated in the years since the service expanded. Group therapy has a wider scope, and various aspects of milieu therapy have been introduced, to augment which the individual recreational and occupational therapy departments have been united into a "therapeutic activities department" with workers being assigned in pairs to each of the inpatient units. The nursing staff has been more actively involved as part of the therapeutic team in work with patients within the hospital, while the social workers have been more active than before in their work with both patients and families.

The Day and Night Center as a treatment modality offers many of the advantages of a half-way house and has been utilized as such for the benefit of a number of inpatients who are improving but not quite ready to live fully outside the hospital. It's described later by Dr. Samuel Feder.

A growing number of patients seeking admission were found to be adolescents, in the age range of 13 to 18, and gradually an Adolescent Division evolved. Although these patients are lodged on each of the inpatient units, they are brought together under the supervision of the psychiatrists of the Adolescent Division, nurses, social workers, and teachers for a number of activities including schooling, therapeutic activities, group therapy, with individual therapy being carried out by residents on the specific wards. The Adolescent Division has its own chief and its corps of staff personnel and preceptors.

An integral part of the psychiatric service once it expanded into its new facilities was a special school of the New York City School system. This enabled both the children and adolescents to continue their education under the guidance of skilled teachers during their period of hospitalization. This service proved of educational as well as therapeutic value for both children and adolescents, often serving as an important bridge between the hospital and the outside community.

Mention should be made that within a couple of years after the start of the inpatient service in 1947, a special follow-up, or aftercare, clinic was developed in the outpatient department, reserved for patients who had been on the inpatient service. This clinic was staffed by both attendings and residents so that the latter would have the opportunity of continuing to treat patients after their discharge.

The research side of the inpatient service has been active from the beginning. By and large, clinical research papers have appeared regularly from the inpatient service as have papers on resident training and the relationship of a psychiatric service to the rest of the general hospital. Some of the first papers published on the effect of hypnosis on dermatologic conditions, on the relationship of somatic disorders to severe psychiatric disturbances, etc. were products of our psychiatry department. Specific research projects including studies of an asthmatic patient (Dr. L. Roose), of a patient with a gastric fistula (Dr. Sidney Margolin), of various aspects of dreaming and sleep (Dr. C. Fisher), and of catecholamine metabolism (Dr. S. Rosenblatt), and others, have all been important contributions by the department. In addition, there have been many publications of specific clinical material and presentations of a variety of studies originating at meetings both within the department and elsewhere.

Throughout the 25 years of its existence, the inpatient service has remained firmly based on its tripartite division of service, training, and research. That it has not deviated from these goals is a credit to Dr. Kaufman, and is an example of his vision, persistence, skilled handling of personnel and situations, and finally, his determination that nothing but excellence would be accepted in any aspect of the three areas of activity within the department. His clinical knowledge, his ability to contribute at all levels within the department, his grasp of all the activities within the service, together with his vision both in planning and carrying out its manifold functions, and most of all, his ability to stimulate and produce the best from those who work with him has enabled the inpatient service to grow and expand and achieve a level of excellence that is perhaps unequaled in any comparable department in the country. This excellence has been recognized throughout the psychiatric world, and evidence of the standing of the department is found in the fact that staff positions have never been vacant and that resident applications have remained at a high level over the years.

This vision of Dr. Kaufman has never been a static one, and the service of today is not the same as the service of five years ago and certainly not that of 25 years ago. There has been constant change and constant advances made as the nature of psychiatric treatment, education, and research have changed. Dr. Kaufman has worked unceasingly for the betterment of the service. When it became evident that a completely voluntary staff was no longer adequate to cope with a vastly expanded service, he was able to obtain sufficient funds from various sources to put part-time paid individuals in certain key positions. This led to further changes and alterations in the general therapeutic training and research programs. While the basic aims upon which the service was founded have not changed, there has occurred a continual search for a better method of their application in light of changing needs of patients, hospital and community.

Adolescent Psychiatric Inpatient Care

RICHARD L. FRANK, M.D.

Adolescent inpatients have been admitted to the psychiatric service ever since Dr. Kaufman assumed the directorship. Since the establishment of the Institute for Psychiatry in 1962, almost half of the applications for admission are for adolescents of high school age, namely, from 13 to 17 years. Young adults, although having much the same problems as the adolescents, are assigned for supervision to the adult service. There are facilities for sharing responsibility with the Child Psychiatry Division for very young adolescents and with the Adult Service for older ones.

Although admission to the psychiatric service in general is mainly in the hands of the chief residents, admission of adolescent patients to what is known as the Jack Martin Adolescent Division* is subject to supervision by staff attending psychiatrists. However, although the staff has a veto power over the admission of particular cases, in practice this has rarely been used. The chief resident screening the patient for admission is normally allowed a great deal of latitude, with the assumption that if a poor choice is made it is possible to have the patient discharged without delay. In practice this is difficult. Therapeutic optimism of young therapists is great and the appeal of adolescent patients is very high. Because of the great demand for beds, the chief residents select patients in terms of the entire Adolescent Division rather than for their own wards.

It is important for residents to have the opportunity of trying out therapeutic procedures with a wide variety of patients. Occasionally cases are admitted for their teaching value even though it is the impression of the senior staff that the therapeutic possibilities for the particular case are not good. This policy does not cause difficulty as long as it is one that is knowledgeably carried out. Difficulties do arise if many unsuitable cases are admitted who do not do well in the hospital and who take up therapeutic time which could be used to better advantage with other types of cases.

Some preliminary work may greatly aid the process of patient selection. Social information obtained at the point of intake helps to clarify the specific treatment needs of the patient. Social workers and social work aides are assigned to investigate applications for admission prior to the screening interview. Home visits and family group sessions with patients on the waiting list for admission are also of great value. Not only do such undertakings help the residents, but they also provide essential contacts with the community. In addition, they facilitate making referrals elsewhere when patients cannot be admitted to the hospital.

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* Subsequent to the marked reduction in the incidence of poliomyelitis grants from the Jack Martin Fund were diverted from the Polio Respirator Service to the development of the Adolescent Division of the Department of Psychiatry. This change of focus was effected by Dr. Horace L. Hodes, Director of the Department of Pediatrics, Dr. Martin Steinberg, then Director of the Hospital, and Dr. Kaufman.

Some cases are admitted solely for work-up, diagnosis, and disposition, in contrast to those who are considered candidates for continuing therapy. The former may involve individuals with borderline intelligence, organicity, and problems involving the adequacy of reality testing. The latter is particularly important where symptomatic treatment of somatic symptoms is being considered. Hospitalization with the possibilities for careful study may be the only way in which it is possible to obtain indications as to the danger of breakdown consequent to the removal of symptoms.

In a similar vein, hospitalization is sometimes initiated to calibrate adequate use of medication. Patients who have not done well outside the hospital may do well under a controlled setting where it is safe to test out medication in adequate dosages. Through careful intake procedures, preparation of such patients for hospitalization and for necessary treatment is carried out.

The policy of a centralized intake procedure for adolescents forces attention upon the problem of the types of cases suitable for hospitalization in a general hospital. Since the hospital presents a completely open setting, without any possibilities of detention, the more floridly psychotic cases are usually referred to hospitals with closed settings, as are cases showing serious sociopathic behavior or acute acting-out tendencies, that is, users of hard narcotics, patients who tend to run away, fire-setters, and serious court cases.

Cases who become acutely psychotic while on other hospital services can be transferred to the psychiatric unit where they are cared for by the use of medication and by intensive nursing during the acute phase. Priority for admission has always been given to patients referred by other services within the hospital, and to private patients of members of the staff, who require emergency hospitalization during their treatment.

It is desirable that the families of adolescent patients have at least one member available for participation in treatment. Hence, it has been expected that the patient and the family live within practical travel distance from the hospital. Needless to say exceptions have had to be made to this, as in the case of patients admitted for physical illness with important psychological concomitants—e.g., ulcerative colitis, asthma, diabetes.

Since psychotherapy, which implies a verbal exchange is the basic therapeutic modality on the service, it has been a desideratum that the patient be able to communicate with the therapist and that communication be possible with the family. The problems presented by the non-English-speaking patient are obvious. It is of note, however, that communication has proved possible in many cases even when a language barrier has been assumed. This is particularly true where there is an understanding of the patient's social and cultural background, and of no lesser importance, where there is a sense of mutual empathy and trust.

The adolescent patients are housed on the adult wards*, where they constitute no more than 15 percent of the patient population or up to four patients per ward at any given time. Each ward has its chief whose responsibility is both a teaching and an administrative one. The ward chief working with the chief resident and the first- and second-year residents maintain the therapeutic functioning of the ward as a whole. The Adolescent Division carries out its responsibility through supervision of the residents' therapeutic work on individual patients. The ward chief takes such responsibility as required by the needs of the entire ward—e.g., if the patient is disturbing the treatment of the other patients on the ward the ward chief has the authority to ask the adolescent preceptor to expedite the discharge of the patient. The adolescent preceptor has the responsibility of guiding, supervising, and teaching the resident how to carry out the best treatment for the individual patient. In principle, in case of a serious disagreement between the ward chief and the preceptor of an adolescent case, the matter can be referred to higher ranking staff for solution, but in practice this has never been necessary.

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* We have not worked out a successful placement of adolescent patients on the Day and Night Center because of time conflicts and the consequent impossibility of coordinating respective programs. Hopefully a solution to this problem will eventually be found.

The preceptor from the Adolescent Division becomes part of the ward to which he is assigned. He attends the ward staff meetings, and in addition, attends the Adolescent Division staff meetings at which activities of that division are coordinated. Since the adolescent patients have their own program in addition to the ward program and since the patients are on four different wards, the problem of coordination is critical.

Dr. George W. Naumburg, Jr. serves as a half-time clinical coordinator for the entire adolescent inpatient division, as well as consultant for the activities program. A half-time junior staff member serves as his assistant. Both make daily rounds to each ward, talking to the nurses, reading the charts, and maintaining liaison with the four ward chiefs and the four chief residents. In addition, a nurse is assigned to the Adolescent Division to coordinate the nursing activities for the patients. Two aides—one male and one female—help to see that the adolescents from different wards participate in the activities program and in the school. The special city school, which is located in the hospital, plays a key part in the whole program.

In the school an attempt is made to evaluate each patient's scholastic abilities and disabilities, to give remedial help when required, and to aid patients to participate in a genuine scholastic endeavor, as well as to participate in the life of their school group. Patients can obtain credit through their own schools for work done at the hospital school, and a number of patients have been graduated and have gone on to college. A major effort is made to correct the frequent misgrading which has previously existed and to get both the patients and their parents to accept the proper placement of the students and to see what expectations are appropriate. The teachers exert an effective therapeutic influence on the patients.

The work with the parents is carried out through social workers who are assigned to each individual ward. Considerable effort is required to see that the resident treating the patient and the social worker who is handling the family are kept up to date with school, ward, recreational, and occupational activities, as well as the patient's behavior on trips of various kinds.

The adolescents meet with the senior resident or other staff member four times a week to discuss their problems in a group. This is not conventional group therapy as such, but it does provide a chance for the patients to get together and to discuss their hospital experience. Another group session is held between the patients and members of the staff at which they discuss jointly problems of the handling of their behavior in the hospital. The adolescent patients also take part in ward group meetings. They are involved in patient representative meetings and are active participants in activities planning. Adolescent staff have to remain alert to prevent the adolescent from becoming involved beyond his current ability in taking over ward responsibilities. The adolescent patients reach out for responsibilities, but frequently are disorganized by them, so that they require a certain amount of protection.

Two staff meetings are held each week in which teachers, social workers, the adolescents' chief nurse and the senior members of the adolescent staff meet to hear about the patients' progress in various areas of functioning. At one of these meetings the residents who are treating the patients are given a briefing as to how the patient is functioning in various areas in the hospital. The resident in turn conveys to the rest of the staff his picture of what is going on with the patient.

A key feature of this part of the program is the effort by staff to provide a structured environment for each adolescent in which he knows his position and is made aware as to what is expected of him and what he can expect from the staff. Staff liaison is a difficult and continuing task. Therapists tend to remain preoccupied with the sometimes fascinating details of the patients' inner life. Both therapy and appropriate disposition are dependent on a comprehensive knowledge of the patient's total behavior.

It has been our experience that whenever the staff becomes upset, and where the structure in which the patient is situated breaks down, a high level of anxiety can be expected on the part of the patients which rapidly builds up until it involves the staff as well. Young staff members readily identify themselves with the adolescents with the consequence that they may view their superiors as opponents. At the same time, when emotional factors force the younger staff persons out of their professional roles, they may react to their adolescent patients as if the latter were indulged siblings who were being allowed "to get away with something." As a result, the responses of the younger personnel may tend to be punitive. To counter this we seek to encourage the latter to ally themselves with their patients, not against some hypothetical oppressor, but against the illness from which the patients are suffering. We attempt to see that in the hospital setting leadership, direction, structure, and treatment replace the reward-and-punishment struggles which not infrequently have characterized the patient's previous experience.

Only the close working relationship and the community of interest between the Adolescent Division staff and the staffs of the individual wards has made it possible for our cumbersome administrative machinery to work. On many occasions the idea has been discussed of setting up a separate "adolescent ward." Many members of the Adolescent Division have favored such a move on the ground that it would be much easier administratively. Up to this point, the idea has been rejected because of the stabilizing effect of adult patients on the adolescent patients and the stimulating effect of the latter on the older patients. Despite its drawbacks, the present system has been made to work so that there has been no continuing pressure to develop a separate ward for adolescents.

Adolescent patients who are admitted to the hospital with external or internal chaotic situations require prompt help in the form of a steady, firm, and structured milieu. The use of appropriate medication serves to reduce the internal chaos. The Adolescent Division prescribes medications at an earlier point than is usual with adult patients. The use of potent medications such as phenothiazines is attempted within the first few days of admission. Dosage is pushed until adequate responses are obtained and then are progressively reduced until the patient is stabilized. Anti-depressants are used where indicated, as are all other appropriate medications. It is the opinion of the Adolescent Division staff that a clear diagnostic and dynamic picture of the level of functioning of the adolescent can be obtained in a brief time and that the early administration of medication does not interfere with such an appraisal. When presented as part of our therapeutic routine, medications are accepted. When medications are introduced at a later time difficulties are often seen because of the several implications of this to the patient. Through close observation of the patient and consistent reporting to the entire staff it is possible to evaluate effects of medications more precisely than would otherwise be possible.

Hopefully, too, the presence of a stable, reliable, and consistent therapist forms a contrast to what the patient has experienced previously. Therapy is designed to help the patient understand the nature and extent of his illness and to provide some clues as to what may possibly be done to help him. A great effort is made to make clear to the patient his assets and his liabilities and to help him understand in what ways he is functioning differently from his healthier contemporaries. In a similar way an effort is made to help him distinguish between his reactions to external pressures and his reactions to internal ones.

As The Mount Sinai Hospital reaches out to its surrounding community, adolescents from minority groups who are suffering from emotional illnesses are drawn into treatment. An inquiry is always attempted to discover what aspect of the patient's behavior and disturbance may be a response to environmental pressure and what part to his personal emotional illness. It is our experience that certain adolescents can exist in very difficult environmental situations without showing signs of illness, although they may show some evidence of anxiety and other mental symptoms. It is also our experience that adolescents develop mental illness just as do individuals in other age groups and that the manifestations of such illness need not be confused with reactions to social stress. Adolescents from all cultures and walks of life have periods of emotional upheaval caused by profound changes taking place during the course of their growth and maturation. It is our firm belief that the signs and symptoms of mental illness can be distinguished as clearly in the adolescent as they can during other times of life. The manifestations of illness may be different in childhood, in adolescence, and in adult life, but they are characteristic for each period.

Our follow-up study shows that outcome is strongly related to types of illness. Of the 75 adolescents discharged yearly, about 60 percent have a discharge diagnosis of schizophrenia, 25 percent of neurosis or situational reaction, and 15 percent of some type of personality disorder. About 30 percent of the patients show significant sustained improvement, while 20 percent have difficulties in the first year after discharge which later tend to recede. Ten percent improve but have some continued difficulties of a lesser degree than on admission. Twenty percent show slight improvement which they fail to maintain, and about 20 percent make very poor adjustment after discharge.

As a general statement, sex and age, as well as type of illness, have a marked effect both on outcome of treatment and on disposition. All schizophrenic boys and schizophrenic girls under the age of 16 tend to do badly. All nonschizophrenic boys and nonschizophrenic girls more than 16 years old do fairly well. The outcome of illness is markedly influenced for the worse by the acuteness of breakdown and by early age of onset.

Length of stay in the hospital is partly a function of the type of illness and partly of the patient's background, but the lack of suitable resources for subsequent disposition has an important influence on this. We are devoting a good deal of effort to making information about such resources more immediately available and to speeding up disposition planning.

A comprehensive adolescent program in a general hospital promotes definitive diagnoses and recommends further disposition as appropriate as community facilities permit. It provides care of acute emergencies arising in the office treatment of patients, as well as for those emerging during medical and surgical treatment in the hospital.

In conjunction with a good aftercare service, it allows effective treatment of a wide range of nonpsychotic patients, especially where changes can be effected with their families. Treatment longer than 90 days is only possible for a few selected inpatients.

The hospital helps many seriously disturbed adolescents and their families through the acute phases of their illnesses. It allows preparation of these patients and of their families for further treatment and helps to get the patients into available facilities.

The provision of emergency help for patients in the surrounding community is a necessary and important service but it presents many as yet only partially resolved difficulties.

An essential function of a program for adolescents in a general hospital is the training of staff. Although it may do this well, the costs are high, and the problems it presents in obtaining prompt diagnosis, treatment, planning, and disposition are great. Ideally these problems are met by the competence of the staff and by close and consistent supervision.

The Adolescent Division at The Mount Sinai Hospital serves as an effective diagnostic and therapeutic facility for suitable cases. It has provided a model for training doctors coming both from adult and child psychiatry in the treatment of adolescents. It has also helped numerous general practitioners to sharpen their understanding of the treatment needs of the adolescent. Hopefully, it has served as a model and as a stimulus for services for adolescents in other general hospitals.

Evolving Patterns of Child Psychiatry in a General Hospital

ABRAM BLAU, M.D.

It seems only yesterday that I was in the Navy, talking with Dr. Harry Weinstock about the new and autonomous Department of Psychiatry that was being established at The Mount Sinai Hospital. Should we go back there, we wondered, or should we reach for the better life in California, Oregon, or the Middle West? That was 1945. Not long thereafter we met Mo Kaufman who had been appointed chief of the new department, and the die was cast. We became his first two adjunct attending psychiatrists. Since then, as others will relate, the staff grew in leaps and bounds, as has the department's space and importance in the hospital with its many separate divisions. Now in 1970, after twenty-five years of his inspiring leadership, it is my privilege to contribute to this volume honoring Mo; it is a task which is entirely congenial to me.

Having had residency training in child psychiatry at Bellevue Psychiatric Hospital with Dr. Loretta Bender, experience as a school psychiatrist with the Bureau of Child Guidance of the Board of Education of New York City, as well as child analytic training at the New York Psychoanalytic Institute, I was assigned to child psychiatry in 1947. It should be noted, however, that there was an active outpatient Child Guidance Clinic already functioning at Mount Sinai Hospital under the leadership of Dr. Wilfred C. Hulse. A child psychologist, Rose Davis, M.A., had been serving the hospital since 1928. Indeed, our hospital had been one of the first general hospitals to become involved in child psychiatry when in 1922 an outpatient Child Mental Health Class was initiated in the Department of Pediatrics under the direction of Dr. Ira Wile. In 1936 Dr. Wilfred Hulse had joined him, and except for an interruption for active military service from 1943 to 1946 in World War II, he continued his devoted work until his untimely demise in 1962.

Historically, general psychiatry has shifted from the state hospital to the community hospital, the clinic, and the private office. Child psychiatry, however, began in the community as child guidance service for the family, the court, and the school, with the emphasis on behavioral problems, delinquency, and learning difficulties. It was, in fact, the child guidance clinic which first evolved the team approach including social workers, psychologists, and teachers. This resulted in a movement away from the medical model and encouraged treatment by nonmedical personnel in social and other community agencies.

These policies probably represented an attempt to avoid inflicting the stigma of mental illness upon the "innocent" child. Indeed, even here at Mount Sinai Hospital, Dr. Ira Wile's clinic catered to this attitude by calling itself a Mental Health Class. Groups of mothers and their problem children were seen together in what must have been one of the earliest attempts at group therapy. Thus, our movement toward a Child Psychiatry Division in a general hospital was actually a unique development, which gave child psychiatry a direct association with clinical medicine and at the same time brought into the hospital the allied disciplines of child psychology, social work, and pedagogy.

The hospital setting adds a valuable dimension to the practice and study of child psychiatry. Here, child psychiatry is more fully concerned with the total child, avoiding the false dichotomy of mind and body, and thus able to regard behavior as the functional aspect of organic structure. The significant aspects of culture and social influences; the contribution of the allied fields of casework, education, nursing, and psychology; and the environmental effects of such institutions as the family, recreation, foster home, and school are also considered fully. In the general hospital, a wide range of varied case material spanning the entire spectrum from birth through childhood and adolescence is found. At the same time, consultation and intercommunication with other medical specialties are readily available, together with the integration of aspects of the community life of which the general hospital is essentially a part.

The most distinctive feature of child psychiatry, as compared with general psychiatry, is its greater involvement with the developing organism. In childhood, character traits and symptoms are in statu nascendi; developmental arrests and fixations are more recent; and regressions go back a shorter distance in time. Diagnosis and treatment involve not only the psychiatric problem itself but also the evaluation of the growing personality in the soil of family, home, school, and social environment. The general hospital setting makes it possible to study the varied reactions of children to physical illness, hospitalization, and psychosomatic disorders, as well as manifestations of psychoneuroses, psychoses, and personality disorders. In turn, the poetic truth that the child is father to the man casts new light on our understanding of adult psychiatric disorders.

Following the pattern already laid out by Dr. Kaufman, it was planned to develop a division of child psychiatry which would work closely with the Department of Pediatrics. Staffing, too, differed from most other child guidance and child psychiatry settings in that it involved part-time voluntary psychiatrists who were in private practice in the community. This was an attempt to structure the department in the traditional medical mode where physicians donated their time to teaching and to giving service to the hospital. Gradually, the Division evolved to include inpatient and outpatient pediatric liaison services, the newborn and premature nurseries, maternal mental hygiene in preparation for childbirth, adolescent liaison on the medical and surgical services, consultation in the emergency pediatric clinic, in addition to the classical long-term and short-term child psychiatry outpatient services, as well as inpatient child psychiatry. We also moved into the field of education, first establishing a postgraduate two-year residency training program in Career Child Psychiatry supported by the National Institute of Mental Health, and secondly, undergraduate seminars and bedside clinics on individual pediatric psychosomatic patients. Subsequently, the Adolescent Psychiatry Division was established as a separate entity. It is described in another chapter by Dr. Richard Frank.

SERVICE, SUPERVISION, AND TRAINING

The complementary relationship between service to patients and training of residents and staff is often a problem. Of course, we wish to give as much service as possible, both in quantity and quality. The resident needs to see a variety of clinical material, but must not be overburdened. The community requests for child psychiatric services are so great that no matter how our staff increases, the fact remains that we cannot meet all the needs of the community. A waiting list is unavoidable, but its excessive length makes for additional frustrations. This situation introduces a delicate balancing problem in administrative supervision between the pressure of referrals from the community and the need to control and limit case loads for the resident.

Preceptoring—weekly clinical one-to-one psychodynamic tutorial sessions—is probably the most important educational experience of the residents. Although our theoretical basis is psychoanalytic, our clinical approach is flexible and includes organic, neurologic, and psychopharmacologic considerations. Our staff represents a variety of psychodynamic schools and viewpoints.

Like other child psychiatry training programs, we do not have the final answer about how to conduct this type of teaching. Among the factors that complicate the matter are: the varying emphasis needed in each situation, a consideration of the personality of the resident, his character structure, his readiness to learn, his reaction to the personality and style of a particular preceptor, as well as the issue of counter transference, and the use of supervisory sessions as covert or overt psychotherapy for the resident. To help the preceptors, we hold a monthly evening meeting where problems of supervision are studied, literature on supervision discussed, and experiences exchanged. At these meetings we have used aural and videotapes of the resident conducting therapy and of supervisory sessions with the preceptor. The main conclusion is that the resident should have the opportunity to work with a variety of senior supervisors of different styles, so that he may make many identifications and thereby create his own unique style as a child psychiatrist and therapist.

We believe that descriptive diagnosis is important nosologically for clear scientific thinking and for formulating a treatment plan. The young resident's enthusiasm needs to be controlled from wild speculations and unsubstantiated interpretations. On the other hand, he needs to be helped to recognize and articulate manifestations of transference and counter transference interactions with his patients and with their parents. Although we favor personal psychoanalysis, and allow time for such scheduled appointments away from the hospital, the optimal timing for such an undertaking is not always clear. In any case, as a medical discipline, we insist that attendance to the requirements of the patients and the clinical program has priority.

As in all apprentice training, we have the problem of how much independent responsibility and how much supervision the trainee should be given. A proper balance between service and training must be considered, avoiding the exploitation of the trainee for the former at the expense of the latter. He must have enough varied material for wide experience, yet sufficient time for intensive work-up, collateral reading, and reflective thinking. We view his autonomous development as our ultimate goal, and he should be encouraged to take as much independent responsibility as possible. A common pitfall in the teaching situation is the possibility that the teacher may be too directive and controlling, thereby encouraging the student to regress and expect too much spoon-feeding How are these important issues to be resolved? Our policy is to give the trainee as much responsibility as is consistent with his role as the doctor and leader of the diagnostic and therapeutic team. The resident is responsible for the coordination, integration, and direction of the ancillary services. To permit intensive individualized work in the first year, each resident carries only a few inpatient cases (totaling about ten for the year) and sees his patient daily for an hour. In the second year, with a greater emphasis on the out-patient clinics, he sees a greater number of cases less intensively. Seminars are considered more meaningful than didactic lectures.

INPATIENT CHILD PSYCHIATRY UNIT

This unit, established in 1962 as part of our new Institute of Psychiatry, consists of 15 beds for disturbed children up to age 13. The original policy was that these children would be admitted for a period of 90 days, as a shorter period would be inadequate for their study, observation, and treatment, while longer hospitalization seemed more suitable for residential treatment centers geared to chronic cases.

The short-term inpatient treatment of children is a relatively new idea with both advantages and disadvantages. Because of current emphasis on the intact family and the prevalent idea that separation of the child is harmful, many families and child care professionals are often horrified at the suggestion of psychiatric hospitalization. The latter, however, is quite a different matter from pediatric hospitalization. For example, we sponsored and helped to expand parental visiting on the pediatric service from once every two weeks to unlimited daily visiting with resultant benefits for the emotional adjustment of the child and his family and a relief of pressures upon the nursing staff. When this was tried on the child psychiatry unit, however, it resulted in considerable chaos and a policy of limited visiting had to be instituted. The difference is caused by the fact that the psychiatrically disturbed child generally comes from a disturbed family setting, particularly in relation to the mother, from whom a separation provides a salutary respite. At the same time long-term separation must be avoided because our goal is the readjustment and return of the child to the family and community as soon as possible to permit proper growth and development.

Intake has gradually become a responsibility of the residents, each of whom take turns to do selection screenings, supervised by the chief resident, and occasionally by the attending-in-charge of the unit. A policy was evolved to limit admissions and discharges to one case per week, as far as possible, and this more or less fixes the intake to about 50 cases annually. We are trying to encourage the referring agencies to recommend for hospitalization less seriously disturbed children who could benefit more from our intensive program, and then return home. We have made some progress in this regard but not markedly so; over 50 percent of our inpatient cases must still be transferred to residential treatment centers or a state hospital. Moreover, since with our limited staff we cannot undertake after-care on all of the large number of cases, the referring agencies must agree at the beginning of hospitalization of any patient to take back and follow the case after discharge from the hospital. A limit of one discharge and one admission weekly is important because these events disturb the emotional and psychological balance of the integrated group on the unit: discharges are depressing and threatening to the remaining children who are concerned about their own future disposition; admissions call for realignment of the pecking order within the group, identity crises, and new rivalries and jealousies with regard to peers and staff. These readjustments are disturbing but, when limited and dealt with knowledgeably, can have positive, meaningful therapeutic effects.

A valuable development which has worked out quite well is the assignment of each child to his own doctor and his own nurse. It is heartwarming to hear these disadvantaged and rejected children talk about *my* doctor and *my* nurse, with a new sense of possessiveness and identity that enriches the ego in the milieu treatment.

THE NURSE IN CHILD PSYCHIATRY

Child psychiatry in a general hospital highlights the need for revision of the role of the nurse and has required challenging and radical changes to fit her into the therapeutic and diagnostic team. At the present time an increasing number of universities are offering postgraduate masters degree programs in Child Psychiatry Nursing. We oppose the practice followed by many inpatient child psychiatry units, particularly residential treatment centers, of using so-called child-care workers and lay therapists who are not essentially a professional group either in training or function. Furthermore, in our judgment the nurse who is in full-day contact with the child seems best qualified to fill the role, particularly in the hospital setting, of mother-surrogate. Her observations of the child's behavior with adults and peers can be a significant ancillary diagnostic activity. Many children, moreover, need to be taught hygienic habits like dental care, bathing, etc., which help to structure their daily activities. Of special importance is the use of a one-to-one quasi-symbiotic relationship to the nurse, especially with autistic children and others where problems of object relationship are paramount. These hour-to-hour maneuvers are most important complements to the individual psychotherapy by the doctor and the total milieu treatment.

Happily, a new important therapeutic function developed for the child psychiatry nurse in the use of visiting hours. Although parents are in individual casework treatment with social workers, as well as in a weekly mothers' group, during visiting hours parent and child interactions can be objectively observed and new meaningful facts established. In addition, the mother can be helped and taught how to relate better to her child in play and in physical relations, notably by demonstrations of interest and affection. Much of what the nurse teaches must be conveyed by example rather than by verbal instruction. In this way, visiting acquires a new therapeutic dimension in our treatment program.

We have initiated a policy of having the nurse on the unit wear every-day clothes rather than a uniform, based on the idea that she might thereby present a less threatening appearance to the child who may have had memories of a nurse assisting at injections and other painful procedures in the pediatrician's office. Despite this innovation the children had no difficulty in identifying the nurse's professional position of authority and helpfulness. With our children, we found it important that within a framework of kindly sensible permissiveness and freedom, we insist upon respect for others and the avoidance of dangerous play. As the nurses took more responsibility for such limit-setting, the number of accidents and injuries decreased. Eventually each child was assigned his "own" nurse, which helped one-to-one needs and the development of individual identity.

CAREER CHILD PSYCHIATRY TRAINING PROGRAM

Staffing was a major problem in the beginning and more so as we grew into a division. Although we now have a few half-time paid staff psychiatrists and attendings, it has been the policy to use part-time unpaid volunteer psychiatrists for service, supervision, and teaching. At first few fully trained child psychiatrists were available and we accepted general psychiatrists who had special interests in working with children, and who developed their skills on the service through supervision, clinical conferences, and seminars. Many of these people became skilled child psychiatrists. Some have continued on staff as senior attendings, others have gone on to head and serve other clinics and agencies in a paid capacity. Indeed, the training of people for service in the community at large has become one of our most important functions.

It became clear very early that we needed an organized qualified training program. The reason was twofold: the community in general needed trained child psychiatrists, and in order to develop adequately, we would have to train our own staff. The difficulty was that to get financial support from the National Institute of Mental Health we had to show an ongoing program; and to have that we needed students or trainees, who, in turn, needed at least some financial support as residents. In a way, we had to pull ourselves up by our bootstraps. A few trainees stayed for one year with small stipends that Dr. Kaufman was able to supply. Finally, in 1955 we graduated our first two-year full-time trainee, Dr. Elizabeth Kleinberger, who went on to become Board-certified in child psychiatry. Dr. Kleinberger is currently one of our most respected senior attendings, in charge of the Inpatient Unit. The training program that was arranged for her helped set a standard which made it possible for us to be approved as a training center.

At first most of our trainees came from outside our hospital. Since the recognition of child psychiatry as a subspecialty in 1954, and our development of a high quality program, more residents have applied for training from within our own Institute. This has been especially true since Dr. George Gross was appointed coordinator of the training program in child and adolescent psychiatry in 1965. Even though our residents are well trained, many having been chief residents in the division of adult psychiatry, some seem to have considerable anxiety regarding child patients and require at least six months before they can regain their previous level of security and confidence. It is remarkable how novel child psychiatry seems to them, and yet to a man they agree that this experience expands and enriches their perspective not only for children but also for adults and adolescents.

Our two-year program is planned for ten full-time trainees. The first year is spent mostly on the inpatient services, the second, in outpatient clinics. Didactic courses are offered in child psychiatry history, growth and development, clinical child psychiatry, child psychiatry treatment, adolescent psychiatry, group and family psychiatry, psychopharmacology, neurology, interview techniques, school, and education. Monthly field trips are made to visit community facilities. Each resident carries a small case load and has both group and individual supervision with tutorial preceptoring. Continuous treatment case seminars, as well as weekly seminars in clinical child psychology, and casework are attended. In the first year, one hour per week is set aside for observation and participation in our hospital school, while two hours per week are set aside for visits to a neighborhood elementary and nursery school. Weekly clinical conferences presented by each clinical section in rotation keep the staff informed of the wide activities in the division. Child psychiatry grand rounds are held weekly and the residents meet weekly for a case seminar with the director of the department. Special stimulation comes from our practice of inviting an outstanding visiting psychiatrist for a few days each year. Past visitors have included Doctors George Gardner, Leo Kanner, Hyman Lippman, Margaret Mahler, Eveoleen Rexford, Franklin Robinson, Stanislaus Szurek, Othilda Krug, William Langford, J. Cotter Hirschberg, Frederick H. Allen, and Stuart M. Finch.

OUTPATIENT CHILD PSYCHIATRY CLINICS

The outpatient services have evolved into a number of different clinics: the aftercare clinic, long-term clinic, family clinic, medication clinic, and diagnostic clinic, as well as the liaison with the outpatient pediatric and adolescent clinics. Supervision is by various preceptors and social service is available for each case. School and home visits in the community are made when indicated. Our clinics have the advantage of routine pediatric evaluation of all cases, and the availability of further medical study when needed.

LONG-TERM PARENT–CHILD PSYCHIATRY CLINIC

This outpatient service follows the format of the classical child guidance team approach and provides the residents with an individual patient treatment experience of two years' duration. The parent, generally the mother, is in active casework treatment while the child works in play therapy with the child psychiatrist once or twice weekly. In most respects, this clinic is the closest paradigm to the private practice of child psychiatry.

AFTERCARE CLINIC

The aftercare or follow-up clinic involves patients who have had a period of care and treatment on the inpatient unit. Out of necessity, this clinic is kept small. Its purpose is to continue treatment begun on the inpatient service and to help the child and parents readjust to community life. It is reserved for a few selected cases of children who have shown improvement during hospitalization and who give promise of continuing to do so.

DIAGNOSTIC AND CONSULTATION CLINIC

The NIFAST Clinic was devised by Dr. Mortimer Blumenthal. The acronym stands for Non-Intensive Flexible-Adaptive Short-Term Treatment. This special clinic is meant to serve the large numbers of referrals from the community and from the Department of Pediatrics. It began when we started a medication clinic which prescribed a variety of psychotropic drugs on the theory that simple pharmacologic control of anxiety, depression, and hyperkinesis, despite the lack of a total psychotherapeutic and social approach, would give some relief. In theory, this partial therapeutic readjustment was expected to correct the unsalutary ecological imbalance of a child in his family and environment and lead to a healthier equilibrium. The NIFAST clinic carried the idea further, instituting, in addition to medication, spaced short visits of child, parents, and siblings, as well as social and environmental manipulation. This global approach comes close to Community Child Psychiatry. It requires an alert diagnostic approach with perspicacious recognition of minor cues in a field of psychodynamic understanding and application. This new clinic enables our limited staff to offer more service in answer to great community pressure. It also gives a wider clinical experience to our residents.

THE FAMILY CLINIC

This special clinic was established for the introductory training of third-year general psychiatry residents who rotate through our service for a 5-month period. A symptomatic child and his family are assigned to the resident for diagnosis and treatment. Special emphasis is placed on discerning the problems of child development in the family and social setting. New cases are selected for a treatment time limit of five months, with specific treatment goals set up at the initial evaluation. The time limitation is made clear at the start. Many patients improve remarkably and move to a new level of adjustment. Others must be referred for further care elsewhere, either to an agency or to one of our clinics. The resident is asked to be involved with the whole family with little help from social service. The purpose of this experience is to give the resident in the short time available in child psychiatry a clinical overview of parent, child, sibling, and family problems, supplemented by relevant reading of the literature.

LIAISON SERVICES

At first, the liaison services was our principal means of extending child psychiatry into the hospital at large. The wide range of the hospital population made it possible to include prenatal, perinatal, infancy, early childhood and psychosomatic problems on preventative, diagnostic, and treatment levels. The child psychiatrist was given the freedom of consulting on any case on the pediatric service without the requirement of a formal referral. This allowed us to pick up many significant problems which otherwise might not have been referred to psychiatry. Pediatricians are often unaware of the borderline areas where we can make a related cooperative contribution, especially in psychosomatic cases. Pending the development of a separate child psychiatry inpatient unit, one bed, and later two beds, on the pediatric service of Dr. Horace Hodes were generously assigned to child psychiatry. Rounds were made in the newborn and premature nursery, and child psychiatry participated in the Preparation for Childbirth Course in the Obstetrics Department. As previously noted, we were instrumental in radically expanding the visiting policy on the Pediatric service. In addition we helped develop a "Mother Bank," designed to furnish more intensive care and attention to very sick infants; a policy of rooming-in during the lying-in period and for sick infants; and facilities to encourage individualized ("natural") childbirth and breast-feeding. Liaison service offered consultation and brief therapy, together with demonstrations to pediatric residents, medical students, nurses and social workers in mental hygiene and child psychiatry.

As staff developed, separate liaison units and teams for service and training were formed under the leadership of an attending psychiatrist working with second-year residents. These units now include outpatient pediatric liaison, inpatient pediatric liaison, liaison walk-in emergency pediatrics, and a Neonate and Infant Development Unit. The latter serves mostly for teaching residents early growth and development; each resident is assigned a mother-infant twosome to observe during pregnancy, delivery, the lying-in period, and subsequently in monthly home visits for a year; the residents also see older siblings at home, and study families in the Well Baby clinic weekly.

The liaison services focus on mental hygiene and child development, as well as psychosomatic considerations. In this situation, the team approach is expanded to involve both graduate and student nurses.

A Final Comment

One recommendation can be made for an additional sorely needed service, a Day Treatment Program. For five years, we had experience with the day treatment program of the Godmothers League, which we helped organize and supervise until it became an independent community unit. In many ways, as the treatment of choice, this is superior to a 24-hour inpatient program, especially for some children and for others as an aftercare continuation program following inpatient care. In terms of the number of children treated and followed, it is a much less expensive undertaking. Many children who now must go on to long-term residential care might remain at home and in the community if such a facility were available.

In conclusion there is the puzzlement frequently expressed concerning our Division by visitors and at gatherings of child psychiatrists. How has it been possible to conduct a service without a full-time director and with only voluntary part-time attending staff? The answer lies in the dedication and loyalty of our professional staff at Mount Sinai Hospital—a dedication believed to be a lost attribute possessed by doctors of old. In this respect, we were doing only as other services were doing, providing the traditional medical practice of free care to the community. Without that quality it could never have been accomplished. Benefits that accrue to the staff are the enjoyment of meeting with colleagues, seeing a wider range of clinical material than in private practice, learning from each other at conferences, and teaching younger colleagues. Of less importance are the possible referral of patients privately and the opportunity to use the inpatient facilities for private patients. Each person knows his job and responsibilities: and to each of them we owe thanks for whatever success we have enjoyed in developing and expanding child psychiatry at Mount Sinai Hospital. Though we have made considerable progress, each year calls for careful review for assessment of new challenges and for the implementation of new ideas for better service and teaching in the future. Nevertheless, though we are proud of our achievement, it must be granted that the child psychiatry service would be best served by a full-time director and more full-time attendings and teachers, in addition to the voluntary staff.

The Partial Hospitalization Program (Day and Night Center) at The Mount Sinai Hospital

SAMUEL L. FEDER, M.D.

A. THE CONCEPT OF PARTIAL HOSPITALIZATION

The Institute of Psychiatry of The Mount Sinai Hospital of New York was dedicated in early 1962. At that time the use of partial hospitalization in the treatment of the mentally ill was relatively new in the United States. Although such treatment programs had been used in Russia since the early 1930's, it was not until the work of Cameron (at the Montreal Allen Memorial Hospital in 1946) and Moll (at the Montreal General Hospital in 1950) that the guiding principles and therapeutic advantages of partial hospitalization were defined. These workers demonstrated that such programs could successfully treat all types of patients, including many who had been traditionally isolated from the rest of the community; that patients often did better when they retained contact with their families and communities; that there were significant advantages in actively involving the family in treatment rather than seeing the patient as an isolated entity; that it resisted some of the regressive tendencies of full-time hospitalization; and that such regression and dependency were neither necessary nor in the patient's therapeutic interests. The part-time hospital was also seen as "... offering treatment facilities to patients as early as possible in the evaluation of their illness, i.e., prior to their disability reaching the point of making (full-time) inpatient treatment imperative." For almost a decade, Cameron and Moll received little support. Then, in the period 1958–1968, between the first and second Conferences on Day Hospitals sponsored by the American Psychiatric Association, the number of partial hospital programs in the United States increased from 141 to 258. This was a time of considerable numerical growth, but the role of the partial hospital remained uncertain. Despite estimates that perhaps 50 percent of all mental patients might be treated satisfactorily in such facilities, most were seriously under-utilized and were reaching less than two percent of the total patient population. Most were organized as day hospitals only, operating five days a week, associated with state psychiatric hospitals, community mental health centers or veterans' facilities, and serving homogeneous populations, largely from the lower socioeconomic groups and the ghetto areas. Very few were part of general hospital psychiatric services or reached the middle or upper class patients. They were used primarily as transitional stages in the discharge from full time hospitalization, rather than as a treatment of choice. Treatment philosophies varied widely, from those advocating an almost exclusive concern with social rehabilitation and behavioral phenomena, to those using a more traditional approach focusing on psychodynamics, psychopathology, and intrapsychic processes as well. The role of individual psychotherapy was uncertain; some excluded it because of lack of personnel; others felt it had no place at all in programs which were constructed about a system of milieu therapy. Uncertainties about the place of such programs in psychiatric residency training programs were inevitable.

B. THE MOUNT SINAI HOSPITAL PROGRAM

It is a tribute to Dr. Kaufman's foresight and progressive thinking that a presentation by Dr. Albert Moll on "The Day and Night Treatment Center" was included at the Dedication Conference of the Institute of Psychiatry in early 1962. Mount Sinai, a large, private, general hospital, was not part of a catchment area, had a patient population drawn from varied socioeconomic and ethnic groups, and had traditionally been oriented towards an intensive one-to-one psychotherapy program. It was in this setting that Mount Sinai, in the fall of 1963, opened its combined Day and Night Center, at that time under the directorship of Dr. Louis Linn. The original announcement stated its goals: "The Center accepts patients with varying degrees of mental disorders—from the acutely ill to those needing a transition between complete hospital care and home . . . without separating the patient even temporarily from the environment. Day patients continue to spend their nights at home and night patients report daily to work or school."

From its start, the Mount Sinai program has had several unusual features. 1) It is one of the few facilities that offered services seven days a week, 24 hours a day. Thus, a patient in either the day or night program who required 24 hour care (for whatever reason other than the immediate risk of suicide) could receive that care in the same setting and among familiar staff for periods up to three to five days. Patients who found the weekends difficult, without the protective structure of work or school, can remain in the same therapeutic atmosphere at that time. 2) Partial hospitalization has always been seen as one primary modality of treatment, that is, with direct admission as the treatment of choice, rather than as a transition-in or transition-out facility. 3) The treatment program has been guided by the search for an optimum form of treatment for selected patients, rather than one that was "just as good" as inpatient treatment, simply a "holding action," or compensation for shortage of personnel or beds. 4) Since Mount Sinai was not part of a Community Health Center, it did not draw from a single catchment area, but rather from a wide range of social, economic, educational and ethnic groups. It has had a "patient-mix" which has worked well, with shared-benefits, and it has established the usefulness of a partial-hospital program for private patients who continued their individual therapies during their time outside the hospital.

C. SETTING

The physical area is designed to implement the treatment philosophy of the therapeutic milieu, that is, to encourage a variety of group and individual interactions, with maximum staff involvement, in a series of activities pertinent to the realities of living at home or functioning at school or at work. It is an integral part of the general hospital, and has access to the large activities facilities of the Institute of Psychiatry. Two large dormitories with fold-away beds, accommodate 21 sleep-in patients at night, and are convertible to use for group therapy and other activities during the day and evening (accommodating up to 30 to 35 patients).

D. THE TREATMENT PROGRAM

The basic aim of milieu therapy is to "... make certain that a patient's every social contact, and his every treatment experience are ... applied towards realistic, specific, therapeutic goals. [It involves] learning through action and its consequences ..." which may be effective at most stages of a person's life. The recognition that most people who require psychiatric hospitalization have seriously disrupted personal relations leading to a state of social isolation has influenced the basic pattern of the treatment program. The program is dynamically based and is a fully integrated one, which includes group activities, group therapy, individual psychotherapy and pharmacotherapy. In addition to nosological diagnoses and psychodynamic formulations, the staff evaluates behavior patterns in the home, at work, school, in social situations, alone, and in groups. Characteristic patterns of communication are observed and considered in terms of developmental history, intrapsychic mechanisms and symptomatology. One or several members of the treatment team visits the home and family, speaks to the school counselors and looks in at the job. We test the work capacity in our own work-experience program. All these are done throughout the hospital period, at meals, during trips, in group and community meetings, in work planning and task groups, and during leisure time. Any difficulty or rising tension is met with spontaneous "crisis-meetings" with the patients or among the staff. These have a significant role in the maintenance of the milieu. The patients are encouraged and given the opportunity to understand their behavior in relation to their intrapsychic lives in formal group therapy, and in individual therapy, with much opportunity to work on what is happening each day.

It can be seen that the gathering of information and the therapeutic use of such information requires the availability and special skills of the nurse, social worker, and activities therapist, as well as the doctor. Every day (or night) session at the hospital begins with some type of group activity (group therapy, planning meeting, or general community meeting). Similarly, every session ends with a gathering of the patients for a general report of their day. The goal is to establish a sense of belonging to a social unit; it also gives the staff the opportunity to assess the state of the group and the individuals in it. Throughout their time in the hospital, the program offers the patients task-oriented and recreational activities, as well as "trips on the town." In all of these, the patients are expected to plan, organize, make decisions and carry through all types of activities. As might be expected, confrontation with these tasks of everyday life will arouse anxiety, fear, and anger, with symptom exacerbation and frequent "acting-out", consistent with the personal psychological difficulties and behavior patterns of each patient. These are observable and available for therapeutic discussion or action at many levels—patient with patient, patient with any staff member, patient in group and patient in individual therapy sessions with his doctor. The integration of all these observations with all modes of therapeutic exploration, the feedback into self-understanding, and attention to their day-by-day behavior constitutes the ideal functioning and utilization of the therapeutic milieu.

E. THE STAFF

The Mount Sinai program offers these possibilities, with the staff organized in a pattern which has been traditional for its Institute of Psychiatry. There is 24-hour, 7-day-a-week nursing attendance. The nurses are in the vanguard of a treatment team of senior psychiatrists, psychiatric residents, social workers, activities therapists, and nursing aides.

However carefully one plans the setting and the structure of the program, the key to any therapeutic milieu is the functioning of the staff. The success or failure for the patients will depend largely on the knowledgeable, open, and cooperative efforts of this group of people who are able to work effectively together despite their own tensions and those many which are generated by a group of psychiatrically ill, often volatile patients, moving about in a completely open setting, who are also away from the hospital (and hence, from its direct observation and control) for at least half the time. Over 80 percent of our patients are diagnosed as schizophrenic reaction (with or without active psychosis) or depression, often with suicidal ideation and or recent suicide attempt. To cope with such a group—with diverse symptomatology, and changing mood states, and lability of behavior, which tend to disrupt any environment—the staff must have a high degree of understanding of psychological mechanisms and their relation to stress and consequent behavior. Only then can the staff maintain a flexible and protective, yet nonregressive therapeutic attitude. Often the patient can drive a wedge between members of the staff, as he may have done with his family. He can play one off against the other, detect tensions and conflicts in the staff and exploit them, or manipulate the development of such rifts. Thus, it is a common occurrence for the patient to shut off all the staff in favor of the special doctor or the special nurse who is seen as the most powerful supplier of the fantasied magical cure. Setting limits, which is so important for the maintenance of the group integrity, as well as for the protection of the patient against his own impulses and fantasies, is impossible without this type of staff awareness. Similar understanding support is required for the patient who finds the pressure to move away from his posture of illness too stressful, and so becomes more symptomatic. The maintenance of this level of staff understanding and operating is a most important function of the senior psychiatrist in such a unit. In addition he is in charge of teaching, of the ultimate responsibility for diagnosis, of an evaluation of goals, and of planning the individual treatment programs.

All professionals learn new roles in a Partial Hospital Program. The fact that an entire range of activities during the day, evening, and night are utilized, results in the doctors' spending a relatively small amount of time with his patient in comparison to that of the rest of the staff.

The Doctor must learn to give and receive information from the rest of the staff freely. He must depart from the traditional limits of the verbal one-to-one interchange in the privacy of his office, but not give it up entirely, and learn to observe, understand, and react appropriately to his patient in a variety of circumstances; he must learn to hear reports from the other staff members in the same way, and help them to understand, in terms of psychological mechanisms, as well as behavior, and respond with a meaningful and constructive plan of action. He must learn that the others see things he did not, and he must respect these communications. At the same time he has the ultimate responsibility, in his role of psychiatrist, for planning the treatment and for making the final decisions for discharge and further treatment. In terms of psychiatric residency training, it is a time best experienced in the third year, when the psychiatrist can put to use all he has learned about psychopathology and psychodynamics, inpatient treatment, psychotherapy in the clinic, and the comprehensive care of the patient with his family, and in his usual environment.

The Nurse who moves out of her traditional role, is confronted, more than any of the other staff, with long periods of active interaction with patients whose illness has forced them into deviant behavior. She must be open, highly motivated, responsible, able to set limits, and yet she must be flexible. She requires much support in a way that respects her efforts and difficulties. She must learn to give much and get little, especially in hoping for a quick therapeutic response to her hard work and efforts.

The Social Worker has the opportunity to use what she has been trained for, in an atmosphere which is very dependent upon her help. Because the patients spend much of their time in their homes, she must work extensively with the family, considering their needs as well as their relationships with the patients. She visits the homes, sees the family alone or with the patients, offers opportunities for job discussions, and has counseling sessions with groups of families who have a patient-member in the hospital. She is the link to practical help with housing, home-makers, and financial difficulties. At the same time she shares the activities with the patients and the rest of the staff on a day-by-day, hour-by-hour basis.

The Activities Therapist is also involved with patients in groups and individually, and must know how to recognize and deal with symptoms, anxiety and the resultant behavior, as he works with the patients in planning, decision-making, responsibility-taking, and execution of tasks.

In all these areas, the staff roles overlap. Each staff member, whatever his special expertise, is confronted by the same emotional responses, reactions to stress, and behavioral problems. Each must use himself in the milieu as a responsive person, always guided by his understanding of what is going on in relation to an individual patient's particular problems or the atmosphere of the group. All of this must then be directed to, and dealt with in, group meetings, group therapy, and individual therapy. One can understand, then, the high degree of motivation and staff esprit and cohesiveness that is required. One can also understand how, once achieved, it remains very fragile and easily disrupted by competition, blame-placing and personal tensions, especially when there is a particularly ill or disputive patient, or when a failure, or more catastrophic outcome, is the end-result. It is for these reasons that it has always been the policy to have the staff of the Day and Night Hospital meet among themselves daily. In addition, since there are many occasions when patients are staying around the clock, both day and night staffs meet together to share information and plan an integrated approach to the 24-hour care of the patient in question.

F. THE PATIENTS

For whom is the partial hospitalization program indicated? Previous studies have indicated that most patients, except active paranoid psychotics and organically damaged patients, can be treated as well in a day hospital as in the 24-hour hospital and it has been estimated that at least 50 percent of all psychiatric patients can do as well, or better, in such a setting. This is probably the case, provided there is free access to 24-hour care on the unit or ready availability of inpatient hospitalization.

Our experience at Mount Sinai indicates that the diagnostic label is the least important factor in the selection of patients or in the achievement of therapeutic improvement. In any psychiatric hospital setting most of the patients would be diagnosed as schizophrenic, psychotic or severely depressed. This is in agreement with Glasscote's findings that admission to Partial Hospitalization programs depended on the " . . . patient's behavior and his supportive resources outside the hospital. Assuming that he did not carry a serious threat of suicide or homicide, was not so grossly disturbed as to disrupt the program, and had something approaching an adequate place to live, most of the programs would be willing to accept him, without reference to the diagnosis or severity of pathology." Although we have felt that intensive family involvement was desirable, this did not significantly influence the outcome; nor did length of illness or frequency of prior hospitalization.

Other contraindications were minimal. Patients were excluded who were not sufficiently integrated to travel back and forth from the hospital, whose symptoms interfered with such travel (e.g., phobias), or who were unwilling to become intensively involved, at least at the beginning of treatment. Alcohol or other drug abusers were excluded if they used these while on the unit, or who came to the hospital so much under their influence so as to be unable to participate in the program. Suicidal preoccupation, or recent attempt at suicide, did not preclude admission. However, no patient was admitted for whom the primary reason for hospitalization was imminent danger of a suicide attempt. Day patients are required to have a place to stay at night; Night patients must be working or going to school, or seemingly able to do so in the immediate future. The admission to an active therapeutic environment is often stressful. Some want either no help or total help, and are disappointed at the prospects of only partial hospitalization; they manage to get themselves transferred to the 24-hour units. On the other hand, many who have had full-time hospitalization recommended will often demand limited part-time care. Our experience has been that these patients do not do well in a partial hospital program; they are usually avoiding recognition of their illness, and, for the same reasons, are often unresponsive to the program. There are still others whose egos are too disrupted to make the transition twice daily from patient to non-patient status. These patients do much better either with full hospitalization or no hospitalization, than they do with partial care. Most people with severe mental illness have fixed patterns of response and living which, no matter how painful or maladaptive, are nevertheless all they have. Their psyches resist any pressures for change. They prefer to stay where they are, with all the primary and secondary gain this may involve; or they seek a magical, omnipotent, but impossible solution. They are often unable to respond to expectations which are even slightly different. These are the patients who, in addition to the phobic and seriously confused patients, are erratic in their attendance or fail to stay in the program. Any effort to change their particular state is often followed by an increase in anxiety or by some manifestation of further mental decompensation. For this reason it is most important for any partial hospital to be closely associated with a full-time hospitalization facility should such situations, often emergency in nature, arise. Related to this is the observation that those patients who do best in the short time partial hospitalization programs are the ones who are undergoing some recent change in their clinical state—regardless of diagnosis, severity of illness, or length of illness. The chronic, unchanging patient will usually decompensate in, or withdraw from, a therapeutic program which expects even a minimal degree of active participation. This has suggested that future planning should be for two types of part-time facilities: a day hospital, which would provide short term, intensive treatment designed as crisis-intervention for the acute patient; and a day care center providing long term treatment with the emphasis on social and vocational rehabilitation for the chronic patient.

G. RETROSPECT AND PROSPECT

Partial hospitalization programs have been in meaningful existence for about ten years. The Mount Sinai Day and Night Center has been functioning for seven years. Despite the many difficulties in evolving a satisfactory time-payment program, and despite the lack of the anticipated enthusiastic acceptance by the profession and the public (patients), we have learned many things which lead to the conclusion that the concept is a valuable one. It is our expectation that this treatment method will continue to grow and develop in a useful and meaningful way.

We have learned that this treatment program, established originally to take care of large numbers of patients, with minimum facilities and personnel, and designed primarily as programs for low socioeconomic groups, has a far greater range. There are many patients, with varied educational backgrounds and from all levels of socioeconomic and cultural life, who take readily to such programs and seem to benefit from them. A mixture of such patients works very well, where the independently wealthy enter a mutually helpful relationship with those on public assistance, where the third grade drop-out establishes a relationship with the graduate student at the university. We have had unskilled workers, school drop-outs, and harassed housewives work right along with patients who were physicians, nurses, lawyers, artists, intellectuals, and musicians, towards the common goal of helping each other overcome their difficulties.

Some patients have done well with the milieu alone; others responded best from the milieu in conjunction with more intensive group and individual therapy, either with our staff, or with their private psychiatrists, whom they continued to see. We have seen how patients who continue their ordinary daytime activities, looking after their families, or going to work or to school, can get deeply involved in an intensive treatment in the evening.

While the early expectations of a strong demand for a weekend hospital did not materialize, we have come to recognize the prime importance of an evening and night hospital. This part of the program has received the greatest utilization; it has worked exceptionally well for many sick but functioning people who probably would have had to enter full-time hospitalization had this part-time facility not been available. The night hospital is not only a transitional step on discharge from the full-time hospital, but it has been, in our experience, a very valuable primary source of hospitalization for the patient in the midst of an acute crisis. Removal from the stresses of home or from the loneliness of an unshared room enables them to continue at work, at school, or at home during the day. This type of treatment is especially helpful to college students and other young adults who respond favorably to the structured therapeutic atmosphere. It is probable that such an evening and night hospital might find its greatest usefulness on the college campuses. The fact that a patient is able to continue his daytime role might suggest that the usual ambulatory care is all that is required. Our experience suggests that this is deceptive and that many people would be prevented from entering full-time hospitalization were they given this type of treatment early in the crisis stage. Preliminary studies have also shown that using day or night hospitalization as a mode of discharge from full-time hospitalization (up to 25 percent of the total hospitalization period) is followed by results that are as good, if not slightly better, as when the patients are kept on full-time status throughout their hospital stay (using the incidence of rehospitalization as a criterion).

The day and night hospital has also been a valuable experience for residents in training, as well as for nurses and other mental health workers. In such a setting, which is in effect a community health center in miniature, the personnel are confronted with the need for truly comprehensive care of their patients, with involvement with all phases of their everyday and intrapsychic lives. It is here, functioning actively as they do in the milieu, that they encounter the whole range of psychological difficulties and observe and work with the impact of the intra- and extra-psychological factors on patients' behavior, symptoms, and functioning. We believe that such exposure should be a part of every resident's training, preferably in his last year, when he can apply his basic understanding of psychodynamics and psychopathology, psychotherapy and pharmacotherapy to a system of comprehensive care which deals also with the daily problems of life and the reality of behavior. It is an experience which trains him to communicate and to cooperate better with others who have different primary areas of interest and skill.

There is no real conflict between individual psychotherapy and the concept of community psychiatry; rather, it may be that the best work in the community is done by those who are well grounded in individual psychology and have developed the attitude and skills to integrate this knowledge, rather than to stand one approach off against the other. This has importance also in maintaining the level of interest, devotion, and effort that is needed by a staff to make such a program viable. Many partial hospital programs suffer from rapid changeover in staff, or a shortage of the better staff people. We believe that this will be lessened when a truly comprehensive approach is used, which will stand as a challenge and source of interest for the type of worker who does it best.

It has been the common experience that, despite its inclusion as an integral part of the community mental health center concept, partial hospitalization has not received full acceptance. When such a program has started as the primary facility, rather than as an addition to the traditional facility, acceptance and utilization has been better. The Mount Sinai program, starting as it did as an addition to a well established 24-hour hospital with the primary focus on individual therapy, has had to overcome standard expectations on both the part of the hospital staff and the community. Along with other programs, we have had to "sell" the idea repeatedly to the community agencies, the psychiatric staff, and all the usual referral sources. As we learned the validity of the approach we had to share this knowledge with them. This has required repeated personal visits and talks with the community resources and agencies. We continue to make such excursions into the community to offer what we can and to learn more about their impressions of us and what their needs are. In the same way, the staff of the traditional facility must be exposed to and educated in the ways and benefits of a part-time therapeutic milieu program, with its emphasis in integrating all modalities of treatment and resource help.

Located as we are, in a large inpatient hospital, and needing as we do, frequent transfers to the 24-hour service when the clinical state of the patients require it, we are often confronted by frequent references to the "failures" of the program. Yet such a program, if it is to reach the population for whom it is meant, must take chances, and must have "failures." Supportive 24-hour facilities must be readily available, otherwise the partial hospital becomes overly selective to a degree that those patients for whom it was designed are shut out.

The hope for the wide acceptance of partial hospitalization programs has been indicated, at least in an administrative sense, by the requirement that they be a part of every community mental health center. The fact that it can treat patients formerly sent to long-term 24-hour facilities has been demonstrated. Their usefulness as a part of the overall treatment programs for those patients requiring initial full-time care is now also established. The specific aspects of such programs have still to be defined and still await detailed follow-up studies which are in progress. There is still a need for intensive training of all mental health professionals in this mode of operation, where each (nurse, social worker, aide, activities therapist, psychiatrist) brings his particular skill and weaves it into the pattern of the milieu.

If the milieu therapy approach is to have any meaning at all, it must be recognized that its therapeutic program cannot be cramped by restrictions in scope nor hamstrung by an arbitrary setting of limits of time. No program, whether part-time or full-time, is adequate without extensive vocational, social, educational and domestic rehabilitation facilities and opportunities. All efforts must be goal-directed to the real life situation, and all efforts toward changing psychological mechanisms and behavioral patterns must occur in an atmosphere of learning, responsibility and utility. It must be accepted that neither the course nor the treatment of mental illness can be determined by cost procedures applicable to predictable medical and surgical conditions which is the current practice and which represents one of our most serious drawbacks. To define a program in terms of allowable days or visits per year is unrealistic. Emotionally ill people may need a few days, a few weeks, or many months; they may need different things at different times, to cope with psychological problems which, with our present knowledge and methods, are chronic and recurrent. Their illnesses do not respond to the demands of any fiscal calendar. Our experience suggests that were it possible to allow as many or as few days as were needed, at any time, without an eye on the calendar, there would be still less need for long term, full-time hospitalization, and a reduction in the overall cost.

Partial hospitalization, with continued real life involvement and active consideration of the environment in which the patient is living, plus the milieu approach integrated with individual psychotherapy, offers much for the future. A person who requires hospitalization is not often one with an ego healthy enough to enable him to gain mastery and strength through verbal communication alone. The very nature of the pathology requires many forms of communication and many opportunities for testing, learning, and experiencing, with opportunities for limited achievement to help him back from the isolated, retarded, and distorted position he takes in the world. In many ways it is the logical portal of entry for patients considered to be in need of hospitalization. Except in the most extreme cases and the contraindications already noted, it can be a place for initial evaluation where the decision can be made for full- or part-time hospitalization, or outpatient ambulatory individual or group therapy.

The Elmhurst Hospital Affiliation

HARRY I. WEINSTOCK, M.D.

In the early 1960's, it became increasingly clear that the municipal hospitals in New York City were failing to deliver adequate care to the large number of patients they were required to admit. The excessive number of admissions was due, and still is due, to the fact that many of these hospitals are designated "receiving hospitals," which in essence means that they are required to admit all patients who need hospital care in their allotted regions, whether they have available beds or not. Thus, it is typical of the municipal hospitals to find empty beds in the corridors that are moved back and forth to and from the wards depending on the numbers of patients admitted. This picture of the municipal hospital as the "dumping ground" for the other hospitals which have selective admission policies in no small way diminishes the attractiveness of these hospitals as teaching centers and so tends to limit the number of applications for staff appointments by highly qualified individuals. It is not only that the frequent overcrowding (e.g., 44 patients in a 25-bed acute psychiatric ward) makes the ward operation and patient care difficult, but the demands on the resident staff for innumerable urgent duties, interferes somewhat with routine teaching exercises. Fortunately, there is a bright side to this experience for the resident, because he quickly learns that he can effectively deal with all kinds of seriously disturbed patients and he often develops the confidence needed to do so.

In his first year at Elmhurst the resident will see for evaluation over a short time say, a day or two—some 1750 new patients; during the same year he will treat for varying periods of time, up to a maximum of three months, at least 100 patients. Again, in that same year he will see in the course of his regular duty in the Emergency Room a total of about 750 patients, of which number he will admit about 300; some of the remaining 450 will be treated briefly, others will be referred to the Outpatient Department, and the rest will be discharged outright. The total number of patients admitted to this 160-bed service of eight wards is 4500, divided among three divisions: 3500 in the four adult wards, 500 in the women's prison ward, and 500 in the three children's and adolescents' wards.

When, early in 1964, The Mount Sinai Hospital agreed to the affiliation with The City Hospital Center at Elmhurst, the chances are it had but little knowledge of the problems it would encounter. Certainly the writer had little such knowledge. Perhaps if he had, he might well have hesitated to assume the responsibility for operation of its Department of Psychiatry. But the wisdom and confidence shown by some of the Medical Board of Mount Sinai, and Dr. Kaufman in particular, in assuming this responsibility even in the absence of thorough information, has unquestionably been proved in many ways. I shall list a few.

When the affiliation began, there were nine residents on this service; now there are 40. There was no full-time attending psychiatrist on the service—only full-time psychologists and social workers. Since most of the part-time psychiatric staff were here only in the mornings, supervision was largely in the hands of persons other than psychiatrists. This has changed so that now there are two full-time psychiatrists, and many half-time psychiatrists, teaching and supervising not only in the mornings, but in the afternoons too.

In the development of this department Dr. Kaufman has not only given his advice and wise counsel on many major problems, but he has made possible the appointment of a number of his staff to this affiliated department, greatly enhancing the overall teaching level of the program. Through his help, it became possible to establish within three years, an approved full child psychiatry training program which is growing rapidly under the direction of Dr. David Schulman. Prior to this affiliation, the lack of trained child psychiatry staff prevented more than minimal efforts at therapy, most of the efforts having to be directed at problems of disposition. An active therapeutic program is now being carried out in the inpatient and outpatient divisions, with the cooperation of a greatly enlarged staff of child psychiatrists and residents. At this time there are eight residents in child psychiatry, and a staff of eight attending psychiatrists some half-time or more, and some less than half-time. Because of the great demand for children's psychiatric service, it is planned to increase this complement of residents to twelve if funds are available, since more residents are now applying for this training.

This department has been most fortunate in obtaining the full-time services of an experienced clinician and administrator for the outpatient division. There are some 16,000 patient visits a year, with very limited space, and with the necessity for continuous direction, supervision, and teaching to make maximum use of time and space. Dr. William Brown, formerly director of the psychiatric service at the Bronx V.A. Hospital continues to do an outstanding and inspiring job in all areas of this division and has added immeasurably to the welfare of the many patients through his activities. Dr. Martin Dollin, in charge of the inpatient service, is an outstanding clinician and because of his broad experiences in municipal and state hospital procedures, and his legal experience in psychiatry, plays an important role in the daily operation of the complicated clinical and dispositional problems.

In this hospital there is a 27-bed ward that is controlled by the Department of Correction of the City of New York. To this ward are sent all women who are under arrest, or who are being held at the Women's House of Detention for trial, and who show symptoms of psychiatric disorder. During a year, some 500 patients are examined and treated, and appropriate recommendations made, either to a court which is held on that ward weekly, or to other courts. Two psychiatrists devote their full time to these duties with the assistance of one or two residents who rotate through this service. For one who is interested in forensic psychiatry this is an outstanding opportunity to gain excellent experience.

We have been most fortunate in having Dr. Mannuccio Mannucci with us from the beginning of the affiliation. Besides serving as a close associate and advisor, he has been the coordinator and developer of the resident training program. Besides the difficult problems of scheduling residents through the three year program, he has been in close relationship with each of the residents, in this way getting "feedbacks" to help in developing various aspects of the teaching program. He conducts a journal club with them, leads a residents' group, arranges for outside lectures, and organizes staff meetings for review of the training program and its needs.

In the course of the six years of affiliation, the primary objective has been achieved—improved patient care through increased quality and quantity of residents and supervising psychiatrists. It is only in recent years that the adult, and now child psychiatry program can count on adequate yearly numbers of residents and that the opportunities afforded for clinical research here can begin to be plumbed. In spite of space and resident time restrictions, a psychiatrist with considerable clinical research to his credit, Dr. Burton Glick, has recently planned a number of clinical investigations which may be expected to develop in the near future. Not only is he teaching the methodology of clinical research to the residents and interested members of the attending staff, but he is being assisted by six of the residents in various investigations outside of their assigned-time responsibilities.

At various times consideration has been given to an integration, partial or total, of the Mount Sinai and the Elmhurst psychiatric residency programs, but the problems involved were of such significance as to make it unfeasible. However, types of day participation and brief clerkships for medical students have begun, and there is no doubt that the variety of cases seen here by the medical student can be most instructive. Such clerkships will most likely increase as the number of medical students rises in the ensuing years.

Since The City Hospital Center at Elmhurst is a general hospital of approximately 1,000 beds, there is a great need for psychiatric consultation in other departments of the hospital. Under the direction of Dr. Albert Lobel, residents routinely perform these duties, but the development of a liaison service similar to that at Mount Sinai awaits adequate funds and staff. A program has recently been organized whereby chronic patients from Creedmoor Hospital not only have emergency surgery performed here, but also elective surgery. With the joint management of the psychiatric liaison division of this department, and the Surgical, Orthopaedic, and Ophthalmological Departments, patients are being operated upon here, supervised by the liaison psychiatric staff, and returned when convalescent to Creedmoor. This, besides benefiting the patients, has benefited these three departments, as well as Creedmoor Hospital. It has resulted in improved relationships between the two hospitals—our performing these services for Creedmoor has caused Creedmoor, in turn, to more readily accept certain patients from us, decreasing some of the overcrowding.

It might be mentioned at this point that, although the census of the Borough of Queens in 1960 was 1,800,000, the medical directory lists but 40 pages of physicians; while the Borough of Manhattan, with 1,700,000, lists 125 pages of physicians. There is an even greater concentration of specialists, including psychiatrists, in Manhattan because of the many medical schools and teaching hospitals there. The recruiting of experienced teachers would be all but hopeless were it not for the support of Mount Sinai. It is hoped that this department will do its share in improving the training of psychiatrists who will practice in this Borough. At this time, five of our graduate residents are actively participating on our teaching staff in major areas of responsibility.

There are many aspects of municipal hospital operation that are unsatisfactory, to say the least. One of the major ones is the budgetary uncertainty. The development of certain new services to patients has not only been stopped, but others may well be cut back due to further budget cuts. Shortages in social workers and clerical staff, and the abandonment of psychiatric service to the rehabilitation department were recent consequences of these cuts, and considerable doubt exists as to when and whether these services will be resumed.

Another great difficulty is the matter of space and of physical appointments as herein described. This hospital was planned some 30 years ago and completed about 15 years ago. In the intervening time the tranquilizing treatment of acute psychosis has proceeded to the point where patients usually present no serious problems of physical management a few hours after admission. Nevertheless, all the toilet and washroom facilities are built for the highly disturbed and destructive patient, with, for example, no possibility of privacy; toilets are without seats in all of the eight wards. Four years ago, an inspection by the then Health Services Administrator and his architect, engineer, legal counsel, financial advisor, and others, caused such embarassment when these most demeaning facilities were shown to him, that he ordered a "crash program" to modernize these indecent facilities, but no activity along these lines has yet been noted. Just recently, there is indication that modernization may begin in the near future.

To put up a small movable partition takes about a year from the time a request is made until actual installation. It is the accepted practice to expect a five-year interval for a wall of a room to be taken down or built! The reason for this is that all of the approvals for such work have to go through various departments before it finally reaches the Budget Department for final authorization. Perhaps with the decentralization of municipal hospital operations that should follow the establishment of the Hospital Corporation on July 1, 1970, these incredible delays will be obviated. It will not, however, increase the amount of space so badly needed for adequate treatment.

Having listed some of the problems and some of the accomplishments, it can justly be said that the original purpose of the affiliation—improved patient care—has been achieved in large measure. To summarize, with the vision, help, and staff support of Dr. Kaufman, the Department of Psychiatry at this hospital has improved patient care considerably by: 1) greatly increasing (to four-fold) the number of psychiatry residents; 2) organizing a fully approved training program in child psychiatry; 3) organizing the only child development evaluation center for mental retardation in Queens; and 4) establishing group therapy programs in all divisions of the department.

Under discussion are plans for a Methadone program, an enlarged alcoholic program, and a "satellite" clinic in the Steinway community, a move towards further community participation and increased delivery of psychiatric service.

Our graduates are being well accepted in other major teaching institutions for postgraduate training; those ready for the American Boards are passing the examinations; and finally, with rare exception, only letters of praise for the services rendered to patients are being received by the Department.

The Liaison Service

LAWRENCE J. ROOSE, M.D.

With the assumption of the chairmanship of the Department of Psychiatry 25 years ago, Dr. Kaufman was in a position to put into full effect a program that he had conceived of as early as the 1920's and had implemented during his years of service at the Beth Israel Hospital in Boston. This program evolved out of the necessity to bridge the gap between psychiatry and the rest of medicine. At that time little attention was paid to the teaching of psychiatry in medical schools. The young doctor as intern and resident, had little awareness of the interrelationship of psyche and soma, nor did the situation change in his later years. As private practitioner and hospital attending, these early attitudes toward medical practice tended to become more solidified and rigid.

The fundamental issue to the psychiatrist was the imbalance in medical care wherein the major emphasis was placed on symptoms and disease processes alone, rather than upon the entire patient, and where the "organic" approach to illness was largely divorced from consideration of emotional factors. Advances in medical diagnostic skills and therapeutic techniques during the last several decades have tended to aggravate this impersonal emphasis on the "organic-laboratory" approach to medical practice. It was the impression of one of our liaison psychiatrists in the late 1930's that members of all the other clinical services were entirely devoid of any interest in the importance of their patients from an holistic point of view. Whether or not this impression was exaggerated, it was true that in many instances in surgery, medicine or specialty, the patient was spoken of as a number, and appeared to be of no special interest to the doctor as an individual.

That the psychiatrist believed he had something of value to offer his medical colleagues which would enhance the quality of medical care, did not result in automatic acceptance of this knowledge. On the contrary the internist and surgeons often resented the psychiatrist's intrusion into their doctor–patient relationship which they felt they were quite capable of managing on their own. The psychiatrist contributed to this lack of communication by being physically isolated from the general hospital. As long as he remained isolated, the reuniting of psyche and soma was pursued by the psychiatrist with commendable zeal, but with little practical results.

The psychiatrist's entry into the general hospital was the first significant step which brought him into physical proximity with his nonpsychiatric colleagues. He now was more readily available as a consultant. Service in this capacity soon revealed many limitations. On the one hand, the typical consultation request was devoid of helpful information for the psychiatric consultant and, in turn, his note in the chart was scarcely more informative. Too frequently, short notes did not elucidate the problem which the consultee had in mind, and long ones were discursive, replete with psychiatric jargon, confused by illegible handwriting, and short on specificity of recommendations for management.

A real working relationship was established only when the psychiatrist moved his operational base on to the various services of the general hospital. With this move, sustained contact with the attending and house staffs established the identity of the psychiatrist as a participating member of the service. With this step the psychiatric liaison service was born. Although this concept must have been germinating in the minds of at least a few farsighted medical educators, The Mount Sinai Hospital's liaison program was one of the first in this country to achieve viability.

Under Dr. Kaufman's guidance the handful of psychiatrists on liaison duty in 1945 rapidly increased in number. In ten years they more than doubled. In 1953 the liaison service was recognized as a component unit of the department of psychiatry with the appointment of an attending in charge. In 1954 psychiatric residents were first assigned to a tour of duty of one month on the liaison service, although this venture was short-lived. It was reinstituted ten years later and today constitutes a major part of the third-year residency program. In 1964 liaison work was included in the training program for those medical interns who devoted one month to psychiatry. With the aid of an NIH grant the appointment of a half-time coordinator in 1965 drew the entire staff together into a more efficient organization. In the next five years the staff doubled in numbers, so that its 50 member staff now covers every major and most minor services of the hospital including the Emergency Room, the organ transplant group, the coronary and surgical intensive care units, the "life-island," and the hyperbaric chamber. Under the rubric of "psychosomatic medicine," the goals of the liaison program were directed toward service to patients, education for the nonpsychiatrists, and research. It became apparent that too few doctors had a clearly systematized conception of the interrelationship of emotional and physical factors in illness although studies indicated that emotional factors play a major role in as many as 80 percent of patients. It was equally evident that the great majority of such cases had to be handled by the nonpsychiatric physician. He should know what he is dealing with, what he can treat adequately, and which cases should be referred for further treatment to a psychiatrist. Service to patients thus went hand in hand with teaching. The opening of a modest 22-bed inpatient psychiatric facility in 1947, called "Ward A," permitted increased service to the most severely ill patients. In fact, the prime function of Ward A was soon recognized to be that of service to the general hospital. Admission of general hospital patients to the inpatient psychiatric service today at Mount Sinai still has top priority. The most immediate educational step simultaneously involved implanting the ideas that Ward A, unlike Bellevue Hospital, was not to be used as a dumping ground for troublesome patients, but, as a special facility where comprehensive treatment, including psychotherapy, was available for a variety of patients in whom psychic factors played a critical role.

To return to the everyday realities of liaison psychiatry today, it would be naive to assume that the mere appearance of the psychiatrist on the ward so easily and quickly established his usefulness. His acceptance depends on a number of factors including his personality and his ability to function as clinician and teacher. To these efforts he brings considerable experience and skill. From the start it has been the policy to appoint senior psychiatrists to the liaison service. It never was a service where young psychiatrists were exiled to serve out their time until transfer to more prestigious assignments.

The qualifications for liaison work are quite demanding. Assuming that the psychiatrist has the necessary educational and clinical background, his development into an effective teacher requires more than ordinary endowments. Most essential is that degree of flexibility which enables him to deal with a wide range of personalities for whom a variety of individualized approaches must be adopted. He has to learn to avoid using psychiatric terminology, which, however enlightening it may be to him, may present a veil of obscurity and a source of irritation to the nonpsychiatrist. Couched in understandable terms, for those doctors with an open mind and with a sense of obligation for the patient's emotional as well as physical welfare, the psychiatrist's concepts can be considered on their merits. More diplomatic and tactful techniques are necessary for those who are indifferent or even hostile. Equally essential is the ability to wait patiently for an opening to effect "contact," which may take weeks or months, and sometimes never occurs. It is well for the psychiatrist to realize that some physicians, due to their own psychological make-up, will never permit themselves to become involved in the emotional life of their patients. Training in psychoanalysis or at least an analytic orientation might be considered as a fundamental requirement for liaison work.

A thorough knowledge of psychodynamics enables the psychiatrist to clarify such critical factors in the doctor–patient relationship as transference and counter-transference phenomena. From its inception in 1925 as the Mental Hygienic Clinic, this department of psychiatry has always been chaired by psychoanalysts and has maintained that orientation in all spheres of its activity.

It would be ideal if the psychiatrist had prior training and experience in the medical area to which he is assigned. When this is not the case, he must acquire enough familiarity to know what the staff is talking about. The relationship between himself and the staff must be with peers, not between teacher and pupil. If the common goal is the patient's welfare, all doctors can contribute on an equal basis. Ultimate success of the liaison psychiatrist's efforts rests largely on the amount of time devoted to his liaison work and upon his dependability. In actual practice, the limited availability of the voluntary attending psychiatrist compels much ingenuity in putting his time to maximum use. Decisions frequently must be made quickly. On a busy service the psychiatrist cannot indulge in the luxury of evaluations extending over weeks or months.

The answer to the question of what to teach is answered by following the evolution of the basic concepts of the liaison service. Early guidelines indicate that these concepts remain sound today, and that changes are more in the nature of shifting emphasis. Service to patients always has been intimately associated with the teaching of descriptive psychiatry. Patients are chosen for extended discussion who illustrate various diagnostic entities. The clinical pictures of the schizophrenias, depressive reactions, psychosomatic illnesses, and other diagnostic entities are elucidated. Depending upon the amount of data available, the psychodynamic structure of the patient is reconstructed. These considerations lead to a more logical solution of management problems.

The liaison psychiatrist does not differ in his approach from the nonpsychiatrist-physician, whether the latter is an intern, resident, or attending. Many attitudes toward medical care are solidified during the house staff years. The private practitioner and the attending in the hospital are one and the same. It is not likely that standards and the concepts of medical care vary to any extent whether the doctor is treating a private patient or one in the clinic or on the ward. Psychiatric liaison conferences deal with patient management problems which confront intern and attending alike. What is told to a patient with a malignancy, for example, does not depend on the financial status of the patient, on his geographical location, or on the status of the physician. Of course, hospitalization in itself confronts the patient with further problems of which the physician should be aware. It is theoretically possible that a management problem might never arise were it not for the fact of hospitalization. Usually that fact is only an acknowledgement of serious illness, a reality which affects both patient and doctor.

The success of a liaison program depends on several variables which may be mentioned briefly. They include the many factors which impinge on the doctor's practice of medicine and those that influence the functioning of the liaison psychiatrist. The personality of the intern, resident, and attending has to be taken for granted. While little can be done to change it, hopefully we can attempt to utilize to the best advantage those characteristics which tend toward good medical practice. Rarely, do personality problems of the house staff become so overt that the psychiatrist must assume the role of the therapist rather than that of the teacher. As might reasonably be expected, personality types differ as widely in doctors as they do in the average population. As yet, no method has been devised, despite many reliable studies, which proves that this or that type of personality structure predisposes an individual to greater or lesser success as a physician.

Various aspects of the hospital milieu may affect patient management more intensively than individual personalities. Among these is the apparent lack of time. The doctor's schedule is a very busy one which often seems to preclude the time involved in taking a comprehensive case history or simply talking to a patient about himself, his reactions to hospitalization, his illness, and the many varied activities which are parts of any person's life, sick or well. Psychiatrists and others regard bedside instruction as a fundamental to any good teaching program. When the liaison psychiatrist suggests to the doctor that they both interview the patient together, a common answer is, "I have no time." Although it is true that the doctor's time is at a premium, even a few minutes allotted by the surgeon or internist to an occasional bedside interview, may be helpful to both patient and doctor. From this we might draw a conclusion that the psychiatric interview and the comprehensive picture that might be gained thereby have a very low order of priority. It may be that, "I am too busy," serves as a rationalization to justify the avoidance of a confrontation that may be troublesome or difficult for the doctor to handle.

Another factor in the hospital milieu which affects medical practice is what is loosely termed "laboratory medicine." In a literal sense, statistical analysis of the number of the laboratory procedures performed on an average medical unit give substance to the phrase. It must be recognized that since the house staff is there for the purpose of learning, many tests which have little or no bearing on either diagnosis or therapy, are performed in order to further the progress of teaching. One chief resident estimated that only 10 percent of the laboratory procedures done on his service were essential to the patient's health. The atmosphere on any service depends on the standards and procedures set primarily by the chief of service and secondarily by the attending staff. The chief of service who is a "laboratory-" or research-minded man develops an atmosphere which pervades the service. The house staff is not impervious or insensitive to such subtle but powerful influences. The superfluity of laboratory tests impedes good medical care in subtle ways. The laboratory report, rather than the total patient, becomes the focus of interest. The patient becomes an instrumentality for research, more bluntly expressed by the patient as "guinea pig" and sometimes acknowledged as such by the doctor. Even if the feeling of being a guinea pig is not overtly expressed by the patient, this remains in the background as a vague source of potential trouble. Its influence is most difficult to evaluate both because of its elusiveness and the amount of time needed to evaluate such a complaint objectively. This matter can be discussed with the house and attending staffs which will consider it freely enough. But, the issue, if it exists as a reality and not only in the mind of the psychiatrist, is accepted as inevitable and unchangeable. It is part of the price the patient has to pay for good medical care. Tangentially perhaps, one intern referred to this problem by stating that service patients are used to being given orders and so accept the medical program without question. Other members of this house staff were quick to refute such a notion and the implication that advantage might be taken of this sociological characteristic.

The "laboratory" milieu has further consequences. Doctors sometimes offer inadequate explanations to patients about the many procedures they are subjected to. In other instances, patients are too upset to assimilate an otherwise adequate explanation. "But we explained all this to the patient" is the usual assertion, stated with some degree of exasperation when it is disclosed that the patient did not understand what, to the doctors, appeared to be logical and simple. When one considers that virtually any person on being hospitalized, is normally anxious, and many unusually so, even simple, logical, and unhurried explanations may not be comprehended. The paranoid patient may seize on this as fuel to feed his mistrust. The average patient may feel uneasy or more anxious but still confines his reactions within vaguely normal bounds.

The relationships of the various members of the hierarchy from intern to assistant resident, chief resident, junior attending, senior attending, and chief of service is another aspect of the hospital milieu which affects patient care. To the extent that the junior physician's future career depends upon the good opinions of his superiors, he may do or say little which will hinder his career. The intern, resident, or attending may say little in opposition to attitudes about medical care maintained by his superiors. Contradictory opinions are relegated, if voiced at all, to expression in bull sessions with peers. (In the drugstore near the hospital where for some years I lunched, the internists and surgeons damned their superiors and hung them in effigy every day of the week.) Many an intern consciously or unconsciously assimilates the "atmosphere" of his service and thereby avoids confrontation by difficult questions. It is left to the liaison psychiatrist to sense the "atmosphere" and remark on its qualities.

There is a fair correlation between the "laboratory" view of medical care and "anti-psychiatric" attitudes. It is unusual for the attending to expound openly on his anti-psychiatric attitudes. They are usually expressed in various more indirect ways. They can, for example, be heard occasionally during ward rounds. It is still too common an experience to hear the attending physician discuss at the patient's bedside matters concerning diagnosis, therapy, and prognosis. To the extent that the attending is a model to be used by the intern, so then does the latter tend to adapt himself to this bedside manner. Rounds is the most inappropriate place for the attending to express his criticism of junior physicians, in full view and hearing of the patient. The patient is usually closer to the house staff than the attending physician with whom the patient may have the most fleeting contact. Indeed it sometimes happens that the patient does not even know the name of the surgeon who is to operate on him, or at best there may be a brief preoperative contact and similarly a brief postoperative one. To the degree that the patient's well being and progress depends on the confidence he has in his physician, such incidents on ward rounds militate against the patient's recovery. Open discussion before the patient about disagreements in diagnosis and treatment can only increase the patient's anxiety. The point is not that such disagreements should never occur but that they should be expressed elsewhere. All too frequently such a discussion becomes rather heated, with the patient becoming the football tossed about in a power struggle between stronger and weaker opponents. Inevitably the resident staff becomes the target of the attending's feelings of frustration and anger which is vented on the "low man on the totem pole." A seemingly innocuous influence of the hierarchial structure is demonstrated by the attending who refers to his house staff as "boys."

It is evident that, as a teacher, the influence of the liaison psychiatrist is rather restricted. Since his time is limited, in practice his teaching is best directed toward those physicians who presumably are the most malleable and the most receptive to new ideas. We are less likely to alter inflexible attitudes in older physicians. If the younger physician is more adaptable than the older one, the liaison psychiatrist might better devote his efforts to the training of the next generation of attendings.

Taking a medical house staff as a model, the psychiatist will soon be aware of the individual personalities in the group and tailor his approach to each accordingly. Overt or covert hostility, indifference, curiosity, and occasionally sustained interest are the gamut of attitudes confronting the psychiatrist. These attitudes may only reflect responses to the realistic problems involved in coping with the emotional life of the patients or they may reflect characterologic defects or problems inherent in the doctors, and hence more difficult matters with which to cope. What should be clear is that doctors, like everyone else, have feelings, and that they react to their patients, sometimes to the latter's advantage, occasionally adversely. The vicissitudes of the doctor–patient relationship is the focal point of liaison teaching into which a considerable amount of clinical psychiatry is blended. To the extent that the doctor understands his patient, be he a schizophrenic or an emotionally healthy person with appropriate anxieties about sickness, hospitalization, and perhaps surgical procedures, he is more adequately prepared to give good medical care. But people, when they become ill, frequently exhibit intensified emotions—reactions which may range from anxiety to panic, from irritation to rage, and from sadness to deep depression. Not infrequently the doctor, when faced with patients who do not accept the medical regimen with calm and equanimity, counteract with varying degrees of anger. If the doctor is at least aware of his feelings, he may assume the responsibility for them to see to it that they do not obscure his objectivity.

The liaison concept has been adapted to the teaching of psychiatry in the Mount Sinai School of Medicine since its inception. After a quarter century this concept has finally achieved its goal of directly influencing the course of medical education through its impact on medical students in all of their clerkships. This is a most fitting culmination of the long and distinguished service of Dr. Kaufman to medical education. After a quarter century this psychiatric liaison service has developed into the largest one to be found in a general hospital in this country. Its growth, strength and viability are a living tribute to Dr. Kaufman's initiative, imagination, and influence.

Open-Heart Surgery—The Patient's Point of View

RICHARD S. BLACHER, M.D.

The recent advent of heart surgery has brought to the fore the central position of the heart in the mental life of man. Heart transplants occupied the headlines throughout the world at a time when liver transplants would merit a short note in the second section, despite the fact that the liver is an equally vital organ. No other surgery has the dramatic, "all or nothing" quality of heart surgery with its implication of sudden death if the heart should cease its vital pumping even briefly. Throughout history the heart has been treated as a unique organ. The heart of Christ plays a special role for many Catholics; the hearts of saints and martyrs have been venerated as relics; primitive man may eat the heart of man or beast to acquire strength and bravery. Indeed, the origin of the word 'courage' is the Latin word for 'heart,' *cor*. Our language is replete with references to the heart as the seat of emotions (1). Expressions such as coldhearted, lighthearted, heartsick, heavyhearted, heartrending are examples of this.

In the early years of heart surgery, severe postoperative reactions were noted and manifested most dramatically in psychotic reactions (2). In recent years, most cardiac procedures are "open," utilizing a heart-lung bypass pump, and it has been observed that the rate of psychosis, ranging from 15 percent to almost 100 percent, has exceeded by far that seen in closed mitral commissurotomy (3, 4, 5). Various organic and psychological explanations have been put forth to explain this phenomenon—cerebral hypotensive anoxia, micro-embolic and other brain damage resulting from surgery, anesthesia or the bypass pump, as well as age, previous rheumatic disease, the psychological impact of the intensive care unit, and postoperative treatment (3, 4, 6).

Work in our hospital suggests an interplay of all these factors, with a major contribution made by the overwhelming anxiety and sense of awe experienced by the patient once he is safely through the danger of the surgery. A parallel might be made with alcohol intoxication. In convivial surroundings, a low blood alcohol level may be accompanied by a sense of drunkenness, while in the face of an emergency, the same drinker with a higher blood alcohol level may feel and even act more sober. So with the postoperative cardiac patient, who may find that in the face of the awesome reality of open-heart surgery, psychosis may be a congenial refuge, and he may drift into such a state on the cloud of impaired cerebral functioning.

Allowing patients to discuss their emotional reactions to heart surgery has highlighted the fact that while in the main, the physician deals with the patient's heart as a realistic organ, the patient does not; to him the heart is both a reality and a source of rich, and, at times, quite unusual fantasies, which seem often to have a greater significance to him than the realistic aspects of his cardiac functioning.

It was felt that a systematic study of patients' concepts of heart surgery might be useful in understanding postoperative emotional reactions and thus aid in the management of such problems. A pilot study was therefore undertaken.

Method

Thirty patients who had undergone open-heart surgery were selected for interview. The only criterion was an ability to speak English. No attempt was made to select ward or private cases, but in keeping with the current admission rates most of the subjects were from the private service. The patients were interviewed a few days after surgery and seen one or more times for periods usually up to thirty minutes, depending on their postoperative condition. The focus of the interview was on the operative experience, and the patients were asked to describe their conception of the surgical procedure. Care was taken not to suggest ideas to the patients who are characteristically eager to please the medical staff during their stay in the intensive care unit. (Even subtle suggestions are readily taken up; this will be discussed later.) Prior to surgery, the patients had been prepared by the surgeon with a realistic description of his procedure. This was reinforced by a printed sheet describing the heart-lung bypass which would be used when the patient's heart was opened. Twenty-seven patients had valve replacements; three had repair of septal defects.

Results (See Table)

The focus of the interview was on the operative experience—that is, what was done and how. Although the procedure was discussed realistically preoperatively, the information was dealt with by the patient in a manner reflecting his ability to tolerate the concept of "opening the heart," and his ability to deny the procedure. This tolerance extended along a spectrum, with five patients explicitly accepting the "opening" and seven explicitly denying it. Between these extremes was seen a wide range of qualification, evasion, shifting evaluations, and idiosyncratic conceptions. Thirteen of the conceptions could be interpreted as acceptance, and seventeen as lack of such acceptance, although the obvious intrapsychic struggle sometimes made such classification difficult. For example, "I know the valve is inside my heart but I don't know and don't want to know if they opened it", or "The valve is inside the chamber but not inside the heart."

Acceptance

Five patients could express directly the idea that "open-heart surgery" meant the heart was incised. Two others qualified this with expressions such as "logic would insist they open it" or "one might assume so." Other patients were quite evasive, making it clear they did not want to talk about the surgery. One patient who kept changing the subject eventually assumed "they open the heart" and then burst out with "they cut it open like a pineapple."

One patient described that although the valve was outside, the surgeon opened the heart to look for clots. Only one of the three patients with septal defect repairs accepted the fact of cardiotomy. One just never conceptualized it; the third insisted the hole was "in the chest somewhere, but certainly not in the heart." Even among those patients able to accept the concept of opening the heart, there was very little talk of the state of the patient when his heart was opened and he was on the pump. Only a few patients mentioned the "moment of truth" when they sewed up the heart and the doctors waited for it to resume beating. That this would not be discussed is not surprising since this state must be interpreted by the patient as equivalent to temporary death, and even "accepters" would tend to deny this.

Denial

The spectrum of denial showed seven patients who explicitly stated that the heart was not opened since the valve was outside, and ranged through such expressions as, "I didn't believe it was opened," to "the valve is inside the heart but I don't know and don't want to know if they opened it," to "they did their best to help me—I don't ask questions."

For most of the deniers, the expression "open-heart surgery" was explained as meaning "they open your chest and expose your heart". For them, there was a transmural migration of the valve to the outside of the heart despite the surgeon's preoperative explanation. A typical description would be, "they open your chest and expose your heart; then they replace the valve". (How?) "They just fiddle around here and there." (Inside the heart?) "Oh no, they couldn't touch *that* very much."

Removal of Heart

A striking conception held by six patients was that the heart, or heart and lungs were temporarily removed during the surgery. While three patients felt that the heart was then opened, the other three did not. It was striking to hear a patient describe vividly how his heart and lungs were removed and put on a machine. "Then they cut out the old valve and put in a new one." (Inside the heart?) At this the patient gasped, "Oh, no!" and blanched.

That several patients could accept the concept of removal of their hearts during surgery, but not the idea of an incision into it is, to say the least, amazing, and so far is not satisfactorily explained. Perhaps the incising of the organ has too immediate an impact to tolerate. This is supported by the terms used by the patients: "They stabbed my heart," "they had to cut my heart," or the dramatic description of the heart "cut open like a pineapple." Several of the patients were able to reveal their thoughts of removal only with reluctance and some embarrassment and quickly tried to qualify this if the examiner responded with any surprise. "I know it sounds crazy, but this is what I thought." This reaction of trying to appear normal, and to please the examiner in an intensive care unit was also evidenced by several other patients who originally described heart removal. On repeated questioning, after several days, they recounted a rather mundane conception of surgery with removal not mentioned. This observation highlights the difficulty the examiner has in learning the

TABLE 1

	Acceptance of opening heart	Denial of opening heart
Explicit	5	7
Qualified	4	4
Don't want to know about it	0	3
Opened to see clots but not for valve	1	0
Removed heart during surgery	3	3

actual fantasies of a patient he may interview in a medical situation. We have been very much aware that the patient, however sick, still has in mind the effect of his words and actions on his medical attendants; nowhere is this more important than in the intensive care units where his need for care is so urgent and his fear of offending or not pleasing the staff is so great.

Valves

Although the meaning of the valve was not the focus of the interviews, several interesting concepts incidentally came to the fore. While the heart is the organ with the greatest emotional and symbolic significance, the valves have very little or no conceptual meaning or mental representation. Some patients have a relatively realistic idea of what valves in general do, and for many patients a valve is part of a machine, especially an automobile. One patient suggested her heart had too much carbon and "needed a valve job." Another stated, "the valve must be clogged like an auto, and the battery doesn't charge right." One man, an auto mechanic, said that his valve was plastic, "and *so far* was holding up". But not only an auto mechanic might be concerned with the durability of a plastic valve. Several other patients made clear their view that plastic was a rather fragile material, equating the plastic in valves with the plastic in cheap toys and gadgets.

The patients with porcine valves expressed pleasure that they would not have to be on anticoagulants for the rest of their lives but did not express any fantasies concerning the transplantation. This may be the result of: 1.) denial; 2.) difficulty in discussing fantasies; or 3.) the relatively slight conceptual significance of valves. Such a transplantation in an orthodox rabbi might of course present certain problems. One woman with a metal valve expressed the wish that it was stainless steel, but then vigorously denied a fear that it might rust.

The idea that a valve allows something to flow into or from a machine reinforces the concept that the valves are outside the heart and hence the idea that the heart need not be opened in open-heart surgery.

Summary

The difficulty in accepting the opening of the heart seems closely related to the development of postcardiotomy psychosis. The sense of awe attendant on incising this special organ has a profound effect on the patient already struggling with an impaired sensorium, and most of the subjects were unable to accept the position of the valves as *within* the heart. For reasons not clear, several of the subjects found it more acceptable to visualize the removal of the heart and lungs than the surgical opening of the heart wall.

The study illustrates how a procedure which may be explained carefully, can nevertheless be interpreted in different ways by the patient. What the surgeon does and what the patient thinks the surgeon does may be quite different.

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Geropsychiatry in the General Hospital

ALVIN I. GOLDFARB, M.D.

The circumstances favorable to providing geropsychiatric inpatient care at The Mount Sinai Hospital were achieved only after long years of work and hope on the part of the Chief of the Department of Psychiatry, Dr. M. R. Kaufman. His deep interest in and knowledge of the problems of aging was apparent as early as 1940 when he discussed a paper on the subject by Atkins from the psychoanalytic point of view (1). The persistence of his interest in aging and the aged was unmistakably attested to by his having created the geriatric section of his department in 1962, and in his encouraging its subsequent development (2). Today the Mount Sinai Department of Psychiatry serves as a demonstration of the potential of general hospitals for inpatient diagnosis and treatment of mental disorders in old persons. Until about ten years ago voluntary nonprofit general hospitals played only a small role in the delivery of psychiatric care. (At Mount Sinai, many aged persons received psychotherapy during the course of medical care, including surgical or neurological treatment, by the liaison psychiatrist.) In the past decade, however, public "screening" hospitals (in which aged persons were observed prior to "certification," where depressed elderly patients could be treated by drugs or electroshock, and where even those with organic mental syndrome could be helped by modern expanding medical therapeutic efforts) have probably shortened the course of numerous disorders, have dispensed with the need for the transfer of many old persons to state hospitals, and undoubtedly have saved the lives of some others. Simultaneously, as increased facilities for psychiatric care became available in a few voluntary hospitals, more psychiatric beds have become available for old persons. A fourfold expansion of inpatient psychiatric beds in 1963 at The Mount Sinai Hospital made possible additional services for the aged. At that time a section of geropsychiatry was officially designated. This made possible the attraction and admission of many chronologically old persons.

Individuals 65 years of age and over comprised about six percent of the total psychiatric admissions in the years 1962 through 1965, and rose sharply to about ten percent in the period 1966 through 1969.* Included in this group were persons with (a) disorders of affect or thought content arising or emerging for the first time to a significant degree in old age, (b) recurrent mental illnesses, and (c) organic mental syndromes of various types and severity such as commonly occur with aging. The majority of these persons entered for definitive meliorative treatment; a smaller number arrived for clarification of diagnosis and stabilization of behavior in anticipation of the need for long-term protective care elsewhere. By admitting these patients, the hospital offered a new and useful service to the community, and simultaneously provided opportunities for staff training and for gaining information about the identification and treatment of psychiatric problems in old age.

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* The assistance of Rafael Levi, M.D., in the collection of statistics is gratefully acknowledged. I am also indebted to Miss Laurel Sprung and Dr. Barbara Berkman for their "Study of Elderly Psychiatric Patients Admitted to The Mount Sinai Hospital in 1967." Unpublished, 1969.

The increase of over 50 percent in old persons cared for beginning in 1969 was undoubtedly related to their new Medicare-based financial eligibility for psychiatric services in a general hospital. Eligibility for general hospital care, however, does not guarantee that it will be accepted or be available. This is demonstrated by the fact that while the ten percent proportion of patient population is representative of the proportion of old persons in the general population, it is not representative of the large proportion of mentally ill old persons within the chronologically old group, which greatly exceeds the incidence and prevalence of mental disorder in younger age groups. Nevertheless, those old people who are now admitted to the general hospital receive more complete and satisfactory health care services than was generally available in the past or appears to be available elsewhere at present.

In the past, prior to Medicare, 93 percent of first admissions in old age to New York State psychiatric hospitals had organic mental syndrome, often severe, usually with clearly definable associated disorder of mood or thinking. The predominant number of the remaining seven percent suffered from disorders of affect or thought. By contrast, 40 to 60 percent of the first admissions in old age to private psychiatric hospitals, of which few now remain, were of persons with disorders of affect or thought content; those with organic mental syndrome made up the greatest part of the remainder. This accounted for large differences in death rate, recovery rate, and the proportion of persons returning to their homes after hospitalization; furthermore it led to a considerable difference in the experience of physicians who worked or were trained in these different institutions. At the same time many persons with mental impairment, often with associated disorders of mood or content, were admitted to old age homes or nursing homes.* Consequently, the patient population of old age and nursing homes included large numbers of individuals who, from the psychiatric point of view, were indistinguishable from persons admitted to State Hospitals. The best of these homes, for example, the Jewish Home and Hospital of New York, have contributed much valuable information about the diagnosis, care and treatment of mentally impaired old persons.

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* "Old age homes" are voluntary, non-profit, nonsectarian facilities usually endowed, supported, and maintained under sectarian auspices—e.g., the Mary Manning Walsh Home, Peabody Home, The Jewish Home and Hospital, the Hebrew Home for the Aged. They are selective in their acceptance of applicants, have long waiting periods which tend to influence the characteristics of admitted residents, and range in type from small and ill equipped to large quasi-hospital facilities. "Nursing homes," up to the present period, have been private proprietary, poorly staffed institutions which, although relatively nonselective in their admission policies, tend to dismiss problem patients later on. Since the creation of Medicare "extended care facility" and "intermediate care facility" standards have pressed proprietary nursing homes toward quasi-hospital functions which chiefly depend upon the patients' physicians for care and direction. Even more recently many proprietary homes have been moving away from accepting Medicare-financed patients of any kind and toward admitting persons whose private income, or Medicare status guarantees payment.

The differences in the distribution of patients in the populations of different types of institutions reflected different patterns in the search for, and in the use made of doctors, hospitals, and treatment programs by rich as compared to poor persons. Few rich persons with "senile" disorders reached state hospitals, no poor persons with affective disorders reached private sanitoriums, and a relatively small proportion of the poor with "functional" disorders chose to use state hospitals. With family aid large numbers of rich and middle income persons with mental impairment (often associated with physical disability or with functional disorders meshed with physical impairments) "chose" to live in nursing homes or found old age homes which would accept them. Large numbers of mentally ill poor persons, with the help of Old Age Assistance gravitated to nursing homes or to state hospitals. The State Department of Mental Hygiene is now trying to decrease its population of aged persons by "decree" which recommends avoidance of the admission of persons likely to need chronic or lifetime care and encourages the use of "community" nursing homes for its old, "institutionally adjusted" patients. These moves place state hospitals in competition with general hospital psychiatric services for the care of the remediably psychiatrically ill and impose upon the latter the burden of acute care of old persons whose basic disorders require long-term care.

A comparison of the characteristics of chronologically old patients admitted to the Mount Sinai Hospital psychiatric division in the periods before and after Medicare became effective sheds light on how or why patients tend to be sorted out for care. Before Medicare old patients fell into various socioeconomic and medical categories whose treatment appeared to differ accordingly. There were many rich persons with organic mental syndrome; their duration of stay was usually less than thirty days and seemed to be related to their hospital insurance coverage. There were relatively few rich persons with affective disorder, and again, their stay appeared to be related to insurance coverage; it lasted from 21 to 30 days and the treatment was most frequently by electroshock. Poor persons were not uncommon on the service; they were predominantly patients with affective disorder; few had organic mental syndrome. Their stay was longer—from two to three months—and this appeared to be related to the 90-day Community Mental Health Board financial limit for those eligible. The treatment of depression in this socioeconomic group appeared to be by way of drugs and conversation first, and only later, when this did not seem certain to promise recovery within the three month period, was there a turn to electroshock treatment. Also, all patients were not equally exposed to activities or to casework; the rich often received less active "team" treatment because more was left to the private physician who did not always provide it himself or ask for it.

These observations suggest that the psychiatric illness itself is not the sole determinant for hospital admission nor for the choice of treatment. Some additional elements of the sorting process are clear. Then, as now, hospital admission and medical care had social determinants. Community Mental Health Board-supported persons came as service cases who first were screened by residents. Their admission usually required, except for emergencies, a wait of several weeks from the time of application. Residents were more likely to accept the younger, affectively disturbed, "more interesting" and "more hopeful" cases, and individuals who seemed more amenable to psychotherapy. Typically, aged persons with actual or presumed organic mental syndrome were likely to be considered beyond help, and often indeed appeared to be so acutely ill, and so disturbing, as well as disturbed, that they would exceed our capacity to care for them in an open ward setting without special nurses, which unfortunately they could not afford. The rich, conversely, were admitted without screening, on direct referral to semi-private status by their private physicians and usually had the ability to pay for special nurses when required. These observations suggest that money could often gain care which medical requirements alone could rarely command.

The advent of Medicare in July 1966 made for changes in the patient population with a slight but not complete shift toward that group characterized as "the rich." Medicare pays for anyone over 65 who needs inpatient psychiatric care for periods of up to 90 days, separated by "well" periods of 60 days spent out of an institution. However, it does not pay for special nursing. Consequently the admission of aged patients with organic mental syndrome who are ambulatory, active, and disturbed, or who are physically dependent and in need of much nursing care, continues to pose many problems to a psychiatric service with an open hospital orientation. The role of the general hospital in answering the needs of aged persons is not yet clear. At present it is in a transitional state in the development of psychiatric services. What it offers will eventually determine whom it serves. Possibly at some time in the future, services may be tailored to community needs as assayed by population surveys.

Despite the seeming limitations occasioned by financing, the small number of beds available, the biases of families and physicians, and the selection of patients as determined by hospital staff, or as dictated by its facilities and staffing patterns, a highly variegated group of patients has been helped. The wide variety has also been of instructional value to personnel on many levels.

From 1966 through 1969 (Medicare became effective in July, 1966) 418 of the 4,110 patients admitted to the Psychiatric Division of The Mount Sinai Hospital were over 65 years of age, 70 percent as private cases, 30 percent as service patients. In general the private patients were physically more ill and impaired, were older, their stay in the hospital was shorter, and a larger proportion of them had organic mental syndrome. While the ratio of females to males for the total group was roughly two to one, the female to male ratio was slightly higher among private patients. The latter, moreover, were more likely to have a living mate. For the total group, females were more likely to have suffered loss of a mate than males, which for some persons is a factor contributing both to the emergence of depression and to the absence of those protections that might avert the need for institutional care. Service cases, who stayed in the hospital longest, were most likely to require casework. Similarly, the younger, unmarried, and usually female patients were more likely to have had casework aid. In sum, it appears that the richer in money, in family, or in both, the more likely it was the psychiatric hospital admission took place later in life, was of shorter duration, and less frequently enlisted casework aid, despite the more frequent presence of brain syndrome.

As in other divisions of the department, service cases in the Geropsychiatric Division are cared for by residents under the supervision of preceptors, staff psychiatrists, and attending psychiatrists. Private geriatric cases, on the other hand, have their individual physicians. Nevertheless, it has been the private patients who have provided much, if not most, of the teaching material for residents. This has been determined by two factors. First, the tendency of residents in screening to select younger patients reduces the number of beds available for aged service cases. Second, the eligibility of old persons for Medicare-financed hospital care and of a personal physician generally leads to their desire for and selection of the private-patient status. This has led to the development of team approaches to private patients in which residents and caseworkers have been encouraged to take as much initiative and responsibility as the "nonservice" status of such patients will permit. Internists, surgeons, neurologists, and other specialists have all joined in demonstrating how comprehensive care can be brought to patients admitted to a service-case-oriented unit by teams. This can serve equally well as a model for physicians interested in independent private practice, group practice or the delivery of comprehensive care services by a public agency.*

Aside from the care they received many of our older patients served as "experiments in nature," contributing significantly to the clinical experience and knowledge of our staff. A particularly vexing problem especially among old persons is the diagnosis of organic mental syndrome. Some years ago a Mental Status Questionnaire (MSQ) was devised by Kahn, Goldfarb, and Pollack (3), which together with M. Bender's Double Simultaneous Stimulation (Face-Hand) Test have proven valid and reliable aids in making the diagnosis of brain syndrome. An example of the importance of these diagnostic tools is given. Mrs. S., aged 80, was admitted early in 1967 "confused, agitated, suspicious and delusional." The MSQ and face-hand tests, however, suggested that her disorientation and confusion were more apparent than real. Treatment with a phenothiazine and lithium carbonate yielded calming, clearing of the delusional ideas, and clarity of thought. Mrs. S. might be called a case of "pseudodementia;" therapy proved she had a reversible "functional" disorder. Our tests, initially, quickly differentiated her from the group of the seemingly hopelessly brain-damaged persons and helped us avoid an initial diagnostic impression of dementia.

Just as depression can be mistaken for brain syndrome so may excited hypomanic patients be mistakenly diagnosed as "confused" and "demented," as I have reported elsewhere (4).

A converse problem was presented by Mrs. R., a 70-year-old woman, who was admitted because of delusions, which Capgras and Reboul-Lachaux have characterized as the "illusion of doubles" (5). She insisted that her husband was an imposter, apparently because he was no longer the strong and able man she recalled and felt she now needed; she talked in a scattered, short-circuiting fashion, and appeared to be reporting bizarre hallucinations. However tempting it was to make a diagnosis of schizophrenia alone, reliance on the mental status questionnaire score and upon her responses to the face-hand test led to a recognition of her condition as organic. This was confirmed by her response to treatment. A relatively long period of hospitalization and judicious use of medication did not help. Her future course over the years has been one of increasing degree of brain syndrome. Mrs. R. is an example of true "dementia," who might easily have been mistaken for a person with functional disorder. Her organic mental syndrome with elaborations of fear and anger might have been mistaken for a purely schizophrenic disorder recurring in or continuing into old age.

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* I am especially grateful to Dr. Isadore Gerber and Dr. Robert Jaffe for their assistance in implementing much of this team approach in the Geropsychiatric Division.

The "functional" disorders in old age may be thought of as being no different in diagnosis or response to treatment than in younger persons, although they frequently pose puzzling and difficult problems. Mention has been made that, as with younger patients, time and financial considerations may press the staff toward the use of electroshock. In contrast, individual characteristics such as verbal facility, appearance, manner of self-presentation ("warmth," "charm") and a similarity of status and cultural background between patient and doctor may lead to the choice of conversational techniques of treatment, while age differences may augment the likelihood that physical methods of treatment be chosen. Beyond these spurious indications for choice of treatment lie some problems which the geriatric service is attempting to clarify and study.

Electroshock treatment (ECT) is undoubtedly one of the most dramatically effective methods of decreasing the suffering in, and shortening the course of, depression in old people. Furthermore, contrary to some opinions, it does work well even when schizophrenic or overt paranoid features are present. This, however, does not necessarily make it the treatment of first choice. It may be a wise choice in special circumstances, among which are financial considerations or lack of hospital facilities.

Few old people suffering from a recurrence of a depression seek electroshock therapy, although it may have been used in earlier depressions. Often, when such illness recurs, they tend to withdraw, hide their disorder, avoid the physician, and refuse hospitalization if it is recommended. This is in contrast to those old persons whose past depressions were treated by medication, conversation, "environmental manipulation" (such as change of milieu), and the expectant use of hospital care. They may themselves ask for and seek out their "old friend," the doctor, for help in easing or eliminating their distress. This difference does not appear to be explained on the basis of how, for psychiatric reasons, patients are selected for one or the other type of treatment, but rather how a particular treatment affects the patient's view of himself, his personal protectors, and his physician.

In the case of ECT, fear, distaste, and a conviction that the patient will be dealt with over his objections play an important part, for this treatment involves "being handled" in a quasi-surgical fashion, with preoperative preparation, recovery rooms, and a post-treatment confusional state. For many it connotes a condition in which personal control is relinquished, and where physical as well as mental dependence upon others is made overt and total. Thus, management of depressive disorders in the old by way of conversation, supportive, motivating, stimulating milieus and medication appears to be the treatment of first choice. Such an approach permits the evolution of an understanding of the disturbance by the patient and his family together with the development of relationships to medical personnel, which in turn encourage and favor the search for, and good use of, treatment, should the condition recur. Avoided is the need to "pick up the patient repeatedly by the scruff of the neck" and to confine him, often against his will, to a place where "he can be made better." Gained is a personal understanding of a troublesome but meliorable disorder for which there is a treatment that does not do damage to self-confidence and pride. Incidentally, it should be added that when electroshock is used, it should be as much as possible in the context of a personal relationship with a physician. Conversation before and during the course of treatment may aid the patient understand his need for help, and minimize the impression of impersonality.

Lithium carbonate was initially introduced into the hospital in the geriatric patient population. Its use in this age group has provided many clues to the clinical monitoring of lithium efficacy and toxicity. As a safeguard, clinical observation is preferable to dependence upon monitoring by way of blood levels. Because of the rapidity with which toxicity can become manifest in the aged, all personnel have become alerted to lithium-induced lethargy, ataxia, tremulousness, "black-outs," gastrointestinal and cardiovascular symptoms. The woman of 80 years mentioned above provided an early demonstration of the value and safety of lithium in old persons. A review of her life history revealed her disorder to be one of a series of previously unrecognized depressive episodes. Now, after four years on lithium, she is managing well. She has minimal mood swings and no evidence of a significant degree of brain syndrome.

Problems of treatment are common in patients with organic mental syndrome. "Acute" reversible brain syndrome is treated by paying meticulous attention to the medical condition and by the elimination of pain, causes for anxiety or physiologic tension. It is now clear that we can change for the better behavior, mood, and even disorders of thought which occur as complications of chronic brain syndrome. But because the intellectual deficit is a reflection of diffuse brain damage, there is nothing we can do for the basic disorientation, memory loss, and other cognitive defects which characterize the disorder. The geriatric service has tested a number of treatments reported to have value. However, anticoagulants have not been systematically used. This general type of treatment has not seemed to be of value in patients with brain syndrome in whom such drugs (e.g., coumadin) have been prescribed basically because of cardiac or other vascular thrombotic disease. Cerebral stimulants and vasodilators have been of no clearly demonstrable value. Recently, hyperbaric oxygen treatment was reported to show promise (6). Investigation by the geropsychiatric service of the value of this treatment in 16 cases did not confirm its usefulness (7). Familiar but neglected drugs like aspirin, the antihistamines and the amphetamines have proven to be of value as sedatives or stimulants. Old standbys like the barbiturates—when kidney and liver function do not contraindicate them—are demonstrably useful. Caffeine citrate may act paradoxically as a sedative in persons with brain damage. The use of high doses of vitamins C, B_1, and B_2 appears to warrant further study. Much experience has been gained in the use of phenothiazines and related substances, as well as with the tri-cyclic compounds. Some popular old-timers which are frequently advocated as both safe and helpful in the aged, like chloral hydrate, have been retried and found wanting.

In dealing with the aged in the general hospital several matters have become very clear. First, is the importance of meticulous medical attention and management. There are interesting relationships between cryptogenic disease and mental conditions such as depression and paranoid states in the aged. This is true for old persons with or without signs of brain damage. The importance of psychic elaborations as clues to physical disease as well as to personal and social problems remains continuously fascinating. The complaint of one man, for example, about "burglars in the cellar" was undoubtedly related to his fears about the recurrence of a rectal carcinoma. Obsessive concern in another man about "the plumbing downstairs at home" was clearly a reflection of a disturbance in his genitourinary function. The patient with brain syndrome may point to specific problems by way of symbolic elaboration or he may use concrete current concerns to symbolize his more abstract complaints. Multiple physical complaints can often be understood as one aspect of a depressive reaction which usually occurs early and, with recovery, leaves late. On the other hand, the old patient with agitation, aggressivity, and disturbing behavior who may have no physical complaints on examination may show fecal impaction or distention of the urinary bladder related to spasm or to an obstructive lesion. Repeated careful medical examination must be a part of psychiatric care. The importance of physical pain, infection, uremia, anemia, and electrolyte imbalance is well known.

Second, it has become clear that a medical team is necessary to create optimal conditions for psychiatric improvement of old persons. The patient, his family, and others are reassured, supported, and sustained by the knowledge that psychiatrists, internists, nurses, and aides are actively concerned and are working together to supply supervision and care. All are relieved by the realization that if a more precise diagnosis might be disclosed by a special study, e.g., angiography, pneumoencepholography, brain scan, and lumbar tap, it will be performed.

Third, it has become apparent that older persons can be helped most in an atmosphere which recognizes and pays attention to the fear and anger generated by their losses of mastery, which responds to their elaborately disguised search for aid in protective ways, and which encourages utilization of their remaining assets. A schema helpful to all levels of personnel engaged in this approach has been refined by observations made on the service (8, 9, 10, 11).

From the foregoing it is evident that the Psychiatric Department at The Mount Sinai Hospital has pioneered in the field of geropsychiatry. What further developments may be pursued in the future?

First of all, it would be logical to expand services so that they are adequate to the large population at risk in the geographic and ethnic catchment areas of the hospital. Our hospital, after all, serves both a local population and a more widespread group of Jewish persons. The probable number of beds required to provide adequate services to the aged can be calculated now on the basis of the known incidence of disorders in the general population. The number of beds available should vary with time as variable needs are discovered by periodic surveys of the two catchment areas served.

At the same time it may be helpful to have a separate, small geriatric section located geographically within the present psychiatric area. It should be specially staffed by teams consisting of psychiatrists, internists, neurologists, psychiatric residents, a charge nurse, assistant nurses, aides and clerks. From this focal point the staff could share responsibility for other old patients located in the psychiatric department and could also respond to hospital-wide requests for consultations. This unit should overlap with—i.e., supervise and help staff—an outpatient department for chronologically old persons, where its duties might be shared by a large number of attending and resident psychiatrists. There is need for a special team whose primary interest is in the aged, a team capable of "shifting of gears," i.e., making a change in attitude when turning from the young to the old.

Affiliation, through overlapping staff and interchange of patients, with an autonomous "old age home" equipped with a large well-staffed infirmary is another hope. In addition to providing necessary beds for long-term patients such a home could offer special opportunities for staff training and research. It could also provide short-term stay facilities for the special needs of patients whose families from time to time may need a rest or vacation from the task of caring for the old person. A nursing home area for long-term care which is an integral part of the hospital may be developed at some time. To make this a suitable "community" and an area which provides truly comprehensive care, this should either be under the supervision of the department of psychiatry or have a large psychiatric staff complement.

A home care service organization would be a welcome addition to the geropsychiatric service. It could provide premilinary and perhaps prophylactic services for those who await admission, and it could provide after-care services for some who would otherwise need protective care in another institution but who for many reasons can be and would prefer to be at home.

Considerable effort may be required to aid patients and families in finding residential facilities in which the patient is comfortable, about which the family is pleased and which does not excessively burden the community.

Expansion of psychiatric efforts to include the family of the old person has already occurred. But such services need great strengthening. Psychiatrists need to have such efforts recognized as an important public health service, and it should become acknowledged as an essential aspect of psychiatric treatment. Such work requires that time, space, and remuneration be available. In the planning of services there is often a forgetting of how much telephone time, reporting time, time for reassurance, support, and direction are desperately needed. Very often a most useful aspect of the treatment of an old person is the benefits rendered to his family. This is especially true for the dying patient. Psychiatric interest in the dying patient is already great; too little interest has been displayed in his family. Aged patients are frequently slowly dying persons whose problems have wide family ramifications.

Hopefully the attainment of these goals will not have to wait too long; surely their fulfillment will serve to justify the trust of Dr. Kaufman in our efforts.

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Group Interaction and Group Psychotherapy in a General Hospital

AARON STEIN, M.D.

The utilization of the group therapies evolved together with other developments in the Department of Psychiatry at The Mount Sinai Hospital. Dr. M. Ralph Kaufman, Director of the Department, recognized the special value of the group therapies as far back as 1945, and it was largely through his interest and support that they began to be used at Mount Sinai, both as a method of treatment and as a means of illuminating the complex interactions that occur in the setting of a psychiatric ward in a general hospital.

A Review of the Literature

In the context of the present essay it is noteworthy that group psychotherapy had its beginnings in a general hospital. Dr. Joseph H. Pratt, an internist working at the Johns Hopkins Hospital in 1905, began a series of discussions with a group of patients with tuberculosis in an attempt to help them deal with both their physical and emotional reactions to the disease. His descriptions of this "classroom method" published in 1906 (1) is the earliest formal account of the use of group psychotherapy.

Much of the early work in group psychotherapy was carried out in general hospitals along the above lines, but it failed to attract much attention. The same was true of the early work with group psychotherapy in mental hospitals, most of which was done with large groups of patients—ranging from 20 to 500—and involved techniques that might be regarded as questionable, for example, the use of a revival type of meeting (2).

The year 1935 marked what might be called the modern era of group psychotherapy. Based on the pioneer work of Wender, Slavson, and Schilder (2, 3), it departed from the contrived methods of earlier workers and utilized the spontaneous discussions of small numbers of patients—six to ten. While some other formats have been used, this technique, utilizing small groups and spontaneous discussion, has found the most widespread acceptance (3).

Other than early reports of Pratt and his coworkers (1, 4, 5), there are comparatively few papers in the literature that deal directly with the use of group psychotherapy in the general hospital. In several papers, Hadden (6, 7, 8) discussed the subject and stressed the need for integrating it properly with the general therapeutic effort. He also emphasized the need for an adequate preparation of patients and described various ways in which group psychotherapy could be utilized in the general hospital, including the demonstration and teaching of psychotherapy. The use of this method of treatment in general hospitals was also discussed by Shaskan (9) who pointed out its value in dealing with the various group interactions occurring there. Peck and his coworkers contributed similar material (10). Other reports (10, 11, 13, 14) have shown various ways in which this type of psychotherapy may help both patients and staff arrive at a better understanding in dealing with the psychological factors in physical and psychosomatic illnesses. Frank and his coworkers (15, 16, 17) have described some of the problems encountered in the use of group psychotherapy in a general hospital. Similar observations of the interaction of various groups, patients, and staff in a general hospital are described in several other reports (18, 19, 20, 21, 22), together with attempts to channel these toward constructive goals. Finally, the writer has summarized a number of communications dealing with the use of group psychotherapy for the treatment of specific conditions, notably the "psychosomatic" illnesses (23). Additional reports along these lines have appeared from time to time (24, 25, 26), but these have been concerned more with the treatment of specific conditions than with the utilization of group psychotherapy in the general hospital setting.

The Development of Group Psychotherapy in a General Hospital

The development of group psychotherapy at The Mount Sinai Hospital occurred in part because of its usefulness in dealing with the complex relationships that inevitably arise between a large institution and its many and diverse component groups.

Group psychotherapy began here in 1945 (27) with a group of menopausal patients in the gynecological clinic. Two other groups were formed in 1948, one in the Veterans Rehabilitation Clinic, and the other for the treatment of a group of peptic ulcer patients. In 1949, an experimental group composed of outpatients was set up as an initial step in an organized study of group psychotherapy in the hospital. In the following year two other groups of patients from the Follow-Up Clinic of the psychiatric ward of the hospital were formed. Several other outpatient groups were organized during the following year, including one group of young schizophrenic males and a mixed group of men and women with psychosomatic complaints.

In 1951, discussion groups were instituted with the nurses on the psychiatric ward, which meetings while not purposely designed to be therapeutic served nevertheless for the ventilation of certain emotional attitudes and hence constituted a type of group psychotherapeutic experience. This was continued for some time in the form of lectures and group discussions under the direction of an attending psychiatrist or a resident. Several years later, in the "morning group session," which will be described later, nurses functioned both as observers and as participants. Nurses also began to lead several other types of groups, which again will be discussed below.

In 1952, a psychotherapy group was set up for the treatment of patients on the psychiatric ward. This patients' group was continued for only a year and although some favorable results were obtained there was some reason to believe that it introduced some potentially disruptive factors into the already complicated setup of the then small psychiatric facilities in the hospital (28). Accordingly, group psychotherapy was not used again on the psychiatric ward for the next few years.

In 1956, because of an increasing awareness of the usefulness of group therapeutic approaches in dealing with the needs and the interactions on the psychiatric ward, three types of group therapy were begun: 1) small-group psychotherapy, either alone or in combination with individual treatment; 2) a morning group session for all patients on the psychiatric ward (29), led by the chief resident and attended by all members of the ward staff; and 3) institution of group discussions involving the patients' activities: "Great Books" program, mental hygiene films, and others. Because of the effectiveness of the group therapeutic approach to patient self-government, to occupational and recreational activities, and to ward management, its use has been greatly expanded. Many such groups are used on the psychiatric wards and, as will be indicated later, constitute a major part of the therapeutic program.

Similarly, the group approach has been the most important part of the therapeutic program on the Day and Night Treatment Center ever since it was established in 1963 and utilizes the morning group meetings, groups for patient self-government, occupational and recreational activities, various types of ward management, and the treatment of patients with regular small-group psychotherapy.

In 1960, responding to the need of the nonpsychiatric physician for assistance in handling problems relating to medical and surgical patients, group therapeutic techniques were instituted, recalling the early experience of Pratt with tuberculosis patients. With the help of a member of the group therapy division, the first of such groups was set up in the diabetes clinic, under the leadership of one of its members. In subsequent years, similar groups led by nonpsychiatric physicians or social workers were set up in the nutrition, allergy, medical, and obstetrical clinics (30).

The need to help ileostomy patients led to the development, in the 1950's, of the so-called "Q-T Club," which used group discussions to help them adjust to their medical, social, and emotional problems (31). Later, similar "stoma clubs" were established in various regions of the United States and in other parts of the world. In addition, group psychotherapy has been used to treat a number of ileostomy patients (32). Similar therapeutic discussion groups led by psychiatrists or social workers have come to be used with cardiac patients, and with relatives of kidney transplant patients, and others.

Counseling or guidance groups, led by social workers, were set up in the 1960's to help older patients and the chronically ill to discuss and deal with their difficulties. This has proven to be quite helpful and their use has continued (32). What might be termed a special type of counseling group was set up in the past year to help heroin addicts being treated with methadone, by discussing their difficulties in maintaining themselves in this treatment. Similar counseling and psychotherapy groups for alcoholics were set up in our Outpatient Department in the late 1960's.

The necessity for dealing with members of the patient's family led to the use of group therapeutic techniques for parents, spouses, and other family members. Beginning in the 1960's, several kinds of therapy have been utilized here, first with families of inpatients, and later with outpatients. Combinations of family and group therapy have been found particularly useful in dealing with very ill people. These problems have received extensive attention in the literature (34, 35).

This chronological account of the development of group therapy at The Mount Sinai Hospital indicates how, from relatively small beginnings with a few outpatient groups, the group approach has increased and expanded until it is now a major part of the therapeutic program of all sectors of the psychiatric service. It is our impression that the dynamic factors operating in group therapeutic approaches are virtually the same—whether in the general hospital or elsewhere. However, our experience would appear to indicate that these dynamics are particularly applicable to the hospital setting, notably in relation to the needs of the patients and of the staff and their interaction. Such therapeutic approaches include activity groups, therapeutic participation groups, and group psychotherapy proper. In the first, the units are composed in a way that its members can engage in a common activity—e.g., sports, dance, drama, artwork, building. Here the activity itself is the principal therapeutic agent, designed to foster socialization especially among withdrawn or disturbed patients. While there may be discussion in these activity groups, it usually centers around the activity itself and not about the individual members' emotional problems. The members of the group establish a relationship with the leader who is usually a trained mental health worker who strives to help everyone participate as fully as possible.

Therapeutic participation groups are arranged to facilitate the interaction of the members. Here active participation is the essential therapeutic agent, with each member finding a role to fill in the life of the group. This type of group is widely used in the therapeutic milieu of hospitals, day and night treatment centers, and "half-way houses," in order to facilitate the activation and socialization of patients.

While the interaction in such groups may help the patient become aware of some of his feelings, attitudes, and reactions, this program is not designed to focus upon them nor to uncover his underlying psychopathology. On the contrary, the therapeutic effects are obtained largely through activation and stimulation, and result from support and from gratification of interpersonal needs. Ideally, as transference objects, the staff and the other patients act as good parental figures and good siblings, helping patients move actively towards better control and integration of behavior, and consequently towards increased participation and socialization.

In group psychotherapy proper, small units are set up for the specific investigation and treatment of the individual member's psychopathology. The three essential characteristics of such a group are, first, that it relies solely on verbal communication; second, that the individual member is the object of the treatment; and, finally, that the group itself—or more accurately, the group interaction—is the main therapeutic agent. The relationships that are established and the interactions that occur are utilized to further the free flow of group communication. Varying degrees of intensity and uncovering are employed depending upon, among other factors, to what an extent transference material and resistance are interpreted. Consequently, group psychotherapy may run the gamut from a highly searching interpretive inquiry to simple guidance and counseling (36). One factor in determining the general position on this scale that will be adopted by a given group is undoubtedly the relationships of its members to the leader and among the members themselves (37, 38).

There are two distinguishing features that characterize transference phenomena in group psychotherapy: 1) the intensity of the transference directed toward the therapist is lessened; and 2) the transference is split since it is directed toward the other participants as well as toward the therapist.

The first of these which results from the presence of the group itself and the need to share the attention of the leader is facilitated by his limiting his own interaction with individual members of the group. The need to inhibit and deflect the transference from the leader to the other members leads to an increase in the intragroup tension, and hence to intensified transference reactions within the group. Based upon unconscious fantasies, patients play roles in the group, tend to act out and interact with one another, often seeking to get the other patients to do the same in a complementary fashion. The availability of the other members as multiple transference objects who are realistically present, and who will actually respond to transference manifestations, results in interactions which can serve as a therapeutic instrument. This response of one member to another's transference manifestations occurs in a very noticeable fashion in the group session, and a major function of the therapist is to insure that it occurs only in the group session and not outside of it, so that it is available for the therapeutic work. Pathological character traits and attitudes become apparent much more quickly and clearly because of these often unconscious transference interactions and hence are more readily available for therapeutic scrutiny.

Another dynamic factor operative in small groups concerns the emotional ties between the members largely in the form of a number of identifications, the most important of which is a sharing of a common object—the leader, or therapist. As noted above the basic nature of this relationship differs from what takes place in the one-to-one relationship of individual therapy, in that it is lessened in intensity and because the leader or therapist is shared by all the members of the group. As a result, he becomes an idealized figure, often used by the patients as a partial substitute for their own superegos. The transference to the therapist is thereby rendered much less intense and threatening and is felt on a much more realistic level, a process that is also aided by the patients' using each other as transient multiple transference objects.

The presence of a number of patients in the group, and the fact that they themselves assume the role of "therapists," provides numerous stimuli for participation and helps them become aware of many of the emotional reactions and attitudes that are being discussed. This is especially true of the characterological traits and social roles of the patients which are seen much more readily and quickly in the group. Psychological mechanisms such as projection and identification also tend to be manifested in a particularly transparent fashion thereby further promoting the gaining of insight and understanding.

Because of several factors, including a "sharing of guilt," the use of various kinds of spokesmen, and especially because of the substitution of the idealized figure of the therapist for the group members' own superegos, certain rigid superego attitudes may be dealt with more readily than in individual psychotherapy. The opportunity for increased interpersonal contact, its realistic nature and atmosphere, all tend to lessen isolation and strengthen contact with reality, while the nature of the ties in the group, especially the identifications, help the members supply each other with a great deal of emotional support, especially in the area of ego-functioning and the strengthening of defenses.

Candidates for Group Therapy

Applying these ideas to the selection of cases, individuals who might feel too threatened or too anxious in a one-to-one relationship with a therapist may be suitable for group psychotherapy. Furthermore, persons with weak or defective egos, and also those who are relatively isolated and have great difficulty in establishing adequate relationships may feel strengthened and benefited by means of the identification with others and the ego-supportive qualities in the group. Patients with projective tendencies and diminished contact with reality are also suitable for group psychotherapy, as are persons with conflicts related to excessively strict and rigid superego attitudes. More specifically, most "psychosomatic" cases, most character disorders, including those with schizoid and narcissistic characters, "borderline," and certain chronic psychotic and neurotic individuals with underlying characterological or borderline defects, may be suitable for group psychotherapy. In addition to the "psychosomatic" cases, patients with marked somatization of their tensions and those with hypochondriacal trends seem to profit more by group psychotherapy than by individual treatment.

Finally group therapy has sometimes served as an opening wedge for introducing poorly motivated or "emotionally illiterate" persons to the subject of mental disturbance in general and psychotherapy in particular.

The foregoing indicates the most important specific dynamic factors involved in group psychotherapy, several of which are particularly applicable to the treatment of general hospital patients. Identification, together with what Slavson (39) has called "universalization"—that is, the realization that others have the same symptoms and difficulties ("all in the same boat")—can operate more effectively when a group of patients has the same condition, such as diabetes, ileostomy, allergy, and others. The existence of the group and the previously mentioned fact that its members assume the role of therapist and actively seek to help in the treatment, is especially useful in the general hospital where groups of patients with similar conditions can be assembled. The way in which the group, in its psychotherapeutic functioning, can tackle a problem and together work out a solution along realistic and socially acceptable lines, makes it an especially practical, effective, and specific form of treatment. Its simplicity and flexibility make it applicable to many different kinds of groups in different situations. It is also readily available as a research tool for investigating a number of individuals at the same time and focusing on the tensions and reactions underlying a particular condition.

The Therapeutic Potential of the Group Approach

The therapeutic effects of group approaches can best be understood by discussing them in relation to the needs of the patients and the staff and their interaction in the setting of the general hospital.

The nature of that setting will determine many things: the kinds of patients, the nature and goals of their treatment, the time available, the varieties of groups, the type of personnel, etc. In the general hospital, since patients tend to be less severely ill from the psychiatric standpoint compared with patients in a state hospital, and have retained some contact with the community, the emphasis in treatment is somewhat less upon activation and socialization than upon an active, short-term program directed at relatively current crises—the same goal of treatment that applies to most medical and surgical patients.

The goals of the general hospital embrace not only furnishing the most effective forms of treatment to individual patients but wherever possible dealing with them in fairly homogeneous groups presenting similar needs and problems. This had led to the formation of groups of patients; e.g., menopause, peptic ulcer, ileostomy, and others.

Continued observation has confirmed the impression (15, 27) that the general hospital serves as a focal point for several emotionally important relationships. These differ in their conscious and unconscious aspects. For example, while on a conscious level the hospital may be seen as a place where a patient goes for the relief of somatic symptoms and other problems, unconsciously, he often seems to relate to the hospital as if it represented some emotionally important figure. Group psychotherapy has brought these interactions much more clearly into focus and has afforded an unusual opportunity to study and to utilize them. As an example, while the frequent, albeit unavoidable, changing of doctors and other medical personnel both in the wards and in the clinics commonly gives rise to considerable distress and anxiety, the stability of the group milieu may serve to lessen these reactions by providing familiar and supportive relationships during these difficult periods of adjustment.

Similarly, experience with outpatient groups has indicated the complex nature of the patient's need for treatment (27). "At the unconscious level, the needs that bring a patient to the hospital are many and varied. They may include the need to alleviate guilt for being ill, the need for dependent care, the need to find substitutes for emotionally important figures such as parents and siblings, and the need to establish relationships with other persons which would satisfy all the above needs in a socially acceptable fashion . . . . Such unconscious needs enter into the treatment situation in a general hospital far more often than is realized . . . ." In the various groups that have been treated, for the most part group psychotherapy, utilizing the relationships and interactions noted, has often been effective in meeting many of these complex needs.

The concentrated experience in the group psychotherapy clinic has also demonstrated that, as previously noted, these factors often provided a surprisingly successful way of encouraging certain resistive persons to enter into the psychotherapeutic process, and also in helping patients with severe characterological defects to perceive and deal with them (30). It was also found, in the group psychotherapy and aftercare clinics and in the Day and Night Treatment Center, that many severely ill patients could be treated effectively by group psychotherapy alone, with individual sessions being used only in acute situations. The relationships that developed in the group provided a considerable mutual support which, together with identification and the "sharing of guilt," with the realization that others had the same difficulties and with opportunities to help each other work these out, enabled them to use the group therapy very effectively.

In the ward, group therapy also tends to dilute the intensity of the unwieldy and sticky attachments of some patients to their individual therapists; this may be quite helpful to the more severely ill patients teaching them to enter more readily into a psychotherapeutic relationship (28). It also provides important group support for the patient, particularly at the time of discharge from the hospital.

An important dynamic factor occurring in the general hospital setting stems from the needs of the hospital personnel: notably, doctors, nurses, social workers, and psychologists, and, to a lesser degree, clerks, aides, technicians, and others who are less directly concerned with patient care. Here also, there are several groups, each with its own characteristics, traditions, and needs in relation to carrying out its functions as well as in its relationship to the hospital and to other groups (15, 19, 30). The interrelationship of these groups and their needs have a definite and important effect upon the way the treatment of patients is carried out.

The conflicting needs and the lack of communication between various groups of hospital personnel is well known and, in relation to the treatment of psychiatric patients, often leads to the appearance of negative attitudes and "acting-out" among such personnel to an extent that it frequently interferes with the treatment program (15, 19, 40). Recognition of these factors has led to the formation of discussion groups for student nurses, not only for didactic and orientation purposes but also to provide an atmosphere for the ventilation and examination of feelings and attitudes. The morning ward meetings were set up for this same reason, and have served this function not only for the patients but also for the medical staff, residents, nurses, social workers, etc., with better communication and understanding on the part of all concerned.

The "morning group-ward meeting" at Mount Sinai was begun in 1956. A similar meeting has been utilized at other institutions, where it has been called variously "patient–staff meeting," "therapeutic community meeting" (in accordance with the pioneer work of Maxwell Jones (41)), or sometimes simply "the community meeting." An extensive literature has accumulated concerning this therapeutic activity; articles by Vitale (42), and Daniels and Rubin (43) give a useful summary of some of the concepts involved. At Mount Sinai it has been used to advantage both on the wards and in the Day and Night Treatment Center (29, 44). Briefly it helps members of the staff to become aware quickly of the general state of the patients and to alert them to the emotional atmosphere prevailing on the ward. The patients are helped to orient themselves to the ward and to their treatment, and by listening to others, they may be helped to become aware of and to accept their own problems and illness. They may be therefore better able to recognize and express anxieties and other reactions to the ward, to the staff, to other patients, and to such crises as attempted suicide, outbursts of violence, etc. Not the least important, the group experience helps the patients to understand and participate more effectively in their own individual psychotherapy.

Similar types of group discussions are used by the staff to deal with various ward management problems, e.g., "elopements," "passes," etc., to set up patient-government activities, and to facilitate the patients' participation in recreational, occupational, and other therapeutic activities. A noteworthy development in the use of group approaches and interaction on the psychiatric service here has been the increasing number of groups created, as noted above.

Training, Research, and the Future

In 1952, a training seminar of workshop in group psychotherapy was created for all the physicians doing group psychotherapy at The Mount Sinai Hospital. In 1955 a Division of Adult Group Psychotherapy was established, and one of the outpatient clinics in the hospital was set up as a group psychotherapy clinic. Since that time, except for the children's division, all training, research, educational, and other activities, including the treatment of patients by group psychotherapy, has been centered in this division, under the direction of the writer.

The training program in group psychotherapy for psychiatric residents and attendings has been described in detail elsewhere (45). Training continues throughout the entire three-year period of the residency. In the first year, the residents act as participant-observers in the morning ward groups, and receive instructions in theory and practice in group psychotherapy seminars. In the second year, the residents do the group therapy under supervision with small groups on the wards, in the Day and Night Treatment Center, and in the Aftercare Clinic, and also attend a group therapy seminar. In the third year, they administer regular group psychotherapy under supervision to outpatients and also attend a group psychotherapy seminar.

Beginning 1967, a training program in group psychotherapy for graduate psychiatrists was instituted under the aegis of the Page and William Black Post-Graduate School. These students attend a seminar, set up outpatient groups, and do group psychotherapy under supervision.

Beginning with the experimental units set up in 1948 to study the nature of the interaction in group therapy (27), a wide variety of clinical research activities has been undertaken, including work with groups of ulcer (46), ileostomy (32), and elderly patients (30). The use of group therapy to handle special transference problems has been reported (47), as has the work with the morning ward groups (29, 44). Experimental approaches are used in setting up new psychotherapy groups in the clinic (9, 48).

For the future, it is anticipated that there will continue to be increased utilization of groups and group psychotherapy in all divisions of the psychiatric service at The Mount Sinai Hospital. Group approaches have been used and will continue to be used to a larger extent in the community and in the community mental health centers when they are fully established (49). Similar approaches have begun to be used, and their use will be expanded in the treatment of various types of addictions.

Finally, the experience of the past twenty-five years has amply borne out the statement made in the initial report (27) on the use of group psychotherapy at The Mount Sinai Hospital, "... The use of group psychotherapy in a general hospital arose from certain needs occurring in the treatment of patients. Its effectiveness in dealing with these indicates its use will be increased." The relationships and interaction in groups and group therapeutic approaches are a most useful means of enabling patients and staff, in the setting of the psychiatric service of a general hospital, to carry out the most effective treatment.

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Roles and Functions of Clinical Psychologists in the Department of Psychiatry of a General Hospital

FRED BROWN, PH.D.*

As an integral component of the Department of Psychiatry, the Division of Psychology works closely with other members of the diagnostic-therapeutic team in meeting the demands for psychodiagnostic evaluation of patients, independent psychological test contributions to team-oriented research projects, participation in the teaching program, and in maintaining high standards for the inservice training of clinical psychologists. The clinical psychologist in this setting functions primarily as a psychodiagnostician whose professional skills are available to inpatient, outpatient, and liaison services of the Child and Adult Sections of the department. His basic role is best described as that of participant-consultant who makes his contributions as an allied professional to problems of differential diagnosis, character delineation, defensive processes, psychodynamics, and prognostic indications. Referrals for differential diagnosis comprise requests for a distinction between neurosis and psychosis, differentiation within a diagnostic category (e.g., pseudoneurotic, borderline, or incipient schizophrenia), and whether certain symptoms can be attributed to organic or functional etiology. Other cases referred for evaluation involve an estimation of the degree to which the patient can be regarded as a suicidal risk, the status of his coping mechanisms, the quality of his cognitive processes, and the bearing of these factors upon eventual disposition of the case. The documented data of the psychologist are derived from a battery of psychological tests that includes conventionally standardized techniques (such as the Wechsler Adult Intelligence Scale, Wechsler Intelligence Scale for Children), more open-ended instruments that encourage responsive latitude on the patient's part and which are supported by normative and empirically derived principles of interpretation within a framework of personality theory (Rorschach, Thematic Apperception Test), and expressive techniques that highlight unique projections of the patient's conception of himself (human figure and other drawings). Many other tests are designed for specific diagnostic purposes, such as tests for assessing visual motor functioning and visual perception dysfunction.

It might be assumed from the foregoing that psychological testing is a completely "objective" procedure that could, for the most part, be delegated to a sophisticated computer. Such an erroneous assumption could easily arise from a test-centered rather than a person-centered orientation in which the fact that psychological testing is an interaction between human beings is ignored. From the moment he arrives for the examination the patient is regarded as a person in need of help whom the psychologist, as a member of the helping professions, is evaluating for the purpose of obtaining a meaningful understanding of him as a person. The tests are administered within a context of sensitive awareness of the patient's feelings and attitudes and the subtle role interactions that are constantly taking place. The patient is encouraged to be as responsive as possible within the limitations his condition may impose upon him, but to subject him to coercion would constitute a violation of the basic tenets of psychological testing.

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* Head, Division of Psychology, Department of Psychiatry, The Mount Sinai Hospital, New York, N. Y. 10029; Professor of Psychiatry (Psychology), Mount Sinai School of Medicine of The City University of New York, N. Y. 10029.

The data obtained and the interpretations derived from psychological testing within a medical setting cannot and should not be regarded as definitive in their own right. Neither the examiner nor the tests can lay claim to infallibility, any more than such a claim would be made for a great many medical diagnostic techniques. The basic value of psychological test findings lies in their elucidation of the patient's personality structure and functioning, explication of psychodynamic processes, sharpening the areas of focal conflict so that they become more discernible and understandable to the therapist, and above all, their contribution to the fundamental decision-making process by formulating predictive statements. The psychologist's report is presented, not as the ultimate communication of a referee, but as a significant supplement to observations and insights obtained by the psychiatric resident, his preceptor, and allied professionals who have had contact with the patient.

In certain settings considerations of time and other factors make it very difficult for staff to obtain a comprehensive case history with which to supplement and reinforce the psychological data. In such situations, as for example on the liaison service, the psychologist's test findings frequently play a determining role in the evaluation of the emotional and attitudinal aspects of the patient's problem. Even on the psychiatry service, the resident's inexperience and the various patient–doctor interactions that complicate the dual task of assessment and therapy imposed upon the resident makes the psychologist's contribution a valuable and welcome one and a salutary example of group endeavor. There are occasions when the psychologist's findings reverse staff's provisional diagnostic formulation or reorder the psychodynamic pattern in congruence with the patient's history and symptomatology. Both staff and patient are the beneficiaries of such a joint task-oriented approach.

Training Functions

The Division has for many years accepted psychology trainees who are considered for internships if they possess the master's degree in psychology or its equivalent in graduate credits, are matriculated for the doctorate in clinical psychology, and have completed a clerkship that has given them an understanding of some of the problems encountered in the psychological examination of patients. Since 1947 the Division has given certificates attesting to satisfactory completion of a one year internship to 100 trainees who have since taken responsible positions in the profession.

The training program has the following aims: 1. To help the psychology intern acquire competence in the administration and scoring of a broad range of psychological tests and measurements which are utilized for the purpose of evaluating intelligence level, personality organization, operating efficiency, and conflict areas of the patient. 2. To give the psychology intern insight into and understanding of psychodynamic processes which operate in the maintenance of mental health and which are intimately linked with emotional disturbances and psychosomatic disease. 3. To provide intensive training in the detection and elaboration of such processes as they are manifested in a) the patient's behavior, b) his symptomatology, c) his level of operating efficiency, d) his complaints, and e) his potentiality for recovery. 4. To heighten awareness of subtle nuances in the test-battery findings with particular regard for the diagnostic formulation and to relate this to the psychodynamic patterning of the global test results. 5. To inculcate a spirit of cooperation with other members of the team in order to establish a functional conception of professional role and integrity. 6. To consolidate these skills and insights in the psychological report in such a way as to offer other members of the team an organized and intelligible communication which will be of the maximum help in understanding the patient and in planning treatment for him. 7. To stimulate the psychology intern's awareness of research problems in this field by means of didactic presentations, staff conferences, and discussion of cases in specific areas of psychosomatic disease. 8. To provide some training in psychotherapy under psychiatric supervision for the purpose of helping the psychology intern to relate psychodiagnostic findings to the treatment process.

In order to achieve these aims training in the Division of Psychology follows five main lines:

1. One didactic session per week totaling one and one-half hours, from September to June. The content of these sessions varies, but it includes: a) discussion of each test in the total battery, with special reference to scoring layout, and basic principles of interpretation; b) basic principles of psychodynamic psychiatry; c) theoretical problems with reference to learning, perception, emotion, intelligence, and imagination (fantasy); d) detailed case presentations illustrative of particular points in reference to personality and character delineation, diagnostic formulation, defense mechanisms, conflict figures and attitudes, and prognostic signs; e) discussion of treatment problems as these are seen by the therapist in relation to the patient's psychological assets and liabilities; f) detailed consideration of the rationale for agreement and disagreement between psychologist and psychiatrist; g) consideration in detail of problems of differential diagnosis with specific reference to the psychodynamic configuration evolved from the test data.

2. Weekly joint staff conferences attended by psychiatric residents, preceptors, case workers, nurses, occupational therapists, and all who have been involved with the patient who is being presented. These conferences comprise: a) presentation by the resident who is treating the patient; b) contributions from allied personnel; c) presentation by the psychologist of his findings; d) joint discussion of diagnosis, treatment planning, disposition possibilities, etc.

3. At these conferences the psychology intern has the opportunity to correlate his test findings with a detailed clinical presentation by the therapist and to observe the relationship between these findings and possible strategies of therapy. It also enables him to validate predictive statements and, when he is ready to do so, to correlate his material with the case and treatment history and to resolve discrepancies.

4. Personal supervision by members of the supervising staff. Supervisors are appointed upon the basis of outstanding competence, maturity, and ability to sense the needs of the psychology intern in terms of his particular personality and level of professional development. Supervision involves: a) Inspection of the scoring and layout of the test material; b) Detailed discussion of interpretations based upon the test material with specific requests by the supervisor for documentary support for such interpretations; c) Monthly ratings by supervisors of the intern's growth in the understanding of his technique and professional role.

5. Personal conferences with the psychiatrist or resident whose patient the psychology intern has examined. This facilitates communication between team members in an informal setting, personalizes the relationship and permits a more relaxed interchange of ideas and interpretations.

Growth Techniques In The Training Process

In training clinical psychologists as psychodiagnostic specialists, one encounters problems of transference, resistance, and overdependency in the supervisor-intern relationship. While these problems will be handled through the supervisor's training program, certain approaches have been utilized up to this time which promise to be useful in helping the psychology intern gain professional self-esteem and confidence. The steps which have been followed in order to achieve this aim have been as follows: 1. In the initial stage of training the psychology intern is required to bring in his raw data for detailed discussion of test elements and interpretations. 2. Following this, and depending upon the rate at which he progresses, he is required to submit a preliminary sketch of his case which is subjected to close evaluation and criticism. 3. The third phase involves a completed psychological report which is presented to the supervisor and defended by the intern upon the basis of prepared documentation. 4. Finally, when it is felt that the intern is ready for independent work he is exempted from supervision and, while retaining the option of discussing his case with members of the supervisory staff at any time, he is permitted to present his findings or discuss them with the therapist solely upon his own merits.

In this way overdependence is discouraged, self-esteem is increased, and the supervisory relationship becomes less directive and more growth-inducing as an experience.

Other Training Activities

In the psychiatric service of a general hospital where coordinated teamwork is emphasized the training program must of necessity include both formal and informal teaching and training opportunities. These overlap in the teaching of psychiatry residents who are given a series of lectures and case demonstrations over a period of six months by members of the Psychology Division which are supplemented by presentations of psychological reports at departmental staff conferences and by discussions between the psychologist who examined the patient and the resident who referred him. This provides an opportunity for a more intensive and meaningful communication between the two disciplines, with mutual feedback and utilization of skills and insights gained from didactic sessions, preceptor guidance, and staff conferences.

Over more than a decade the Department has conducted an NIMH-supported training course for nonpsychiatric physicians for the purpose of sensitizing the physician to emotional factors in illness with the expectation that such knowledge will enrich his understanding of the patients he sees in his practice and will bring him closer to the humanistic ideal of medical practice. A psychologist was assigned to this program from its inception and has functioned ever since as an indispensable member of the teaching team.

The Head of the Division of Psychology has participated in the teaching of undergraduate and medical students on clerkships in the Mount Sinai School of Medicine. In time it is anticipated that other members of the Division will be called upon to join in the teaching enterprise.

Finally, the psychologist is occasionally asked to give one or two lectures to attending physicians and residents on the medical service for the purpose of acquainting them with his functions and indicating his value as a resource within the institution.

Inconsistencies in Test Findings

The psychodiagnostician's task becomes a very exacting one when he is required to present a logically cohesive and integrated report of his findings to the referring source. The report must approach as closely as possible to definitiveness, with a very minimum of loose ends and unanswered questions. There are two areas in which inconsistencies and incompatibilities will arise; within the test battery and between test findings and the clinical data.

Internal discrepancies must be dealt with in a conservative manner on the realistic assumption that neither the examiner nor his instruments are infallible. Furthermore, the emotionally disturbed patient is likely to project the jarring inconsistencies within his own personality and these need to be taken into account when preparing a reliable assessment of his psychological status.

In order to cope with these difficulties the examiner must carefully scrutinize all test responses in the structured and unstructured instruments, focus upon diagnostic and psychodynamic leads within the framework of valid personality theory, and then, utilizing these relatively "hard" data as elements in the formulation of a working hypothesis, scan adjacent areas within the test battery for connecting links that will reinforce the initial hypothesis. More information is fed into this matrix until a tenable conclusion can be derived from this cross-validative procedure. In approaching this difficult task the psychologist must consider the role played by levels of awareness on the patient's part in making responses to the tests. For example, biographical material may intrude into TAT stories, associations to human figure drawings may be a conscious statement of the patient's self-conception, and even in the Rorschach, metaphorical responses will reflect the patient's basic life thema and the manner in which he is experiencing himself with regard to the status of his illness (e.g., Rorschach Card I, "It's almost as though someone were standing in the center of . . . some terrific expanding force. He's splitting . . . the forces are almost too much for his control, the expanding forces . . . as if he's pulling in against the force which had once been contained in him . . . I don't know if he's about to lose control", given by a 20-year-old brilliant patient, very suicidal, and in a state of rapid decompensation). What comes from the most conscious level of the personality (e.g., patient laughs when given TAT picture of man standing with hat in hand and stern looking woman with back turned to him looking out of the window, "That's the way it is with me and my mother") will often differ markedly from content and defenses related to preconscious and unconscious sources.

The issues involved in dealing with discrepancies between a) the psychologist's findings and diagnostic formulation and b) the psychiatrist's clinically derived conceptualization of the case are succinctly delineated in the following statement (1):

> Incompatibilities between test findings and the clinical picture arise from sources already mentioned as well as others, but such discrepancies should not immediately disconcert the clinician and stampede him into rejecting his findings. For one thing, we do not yet understand completely the relationship between modes of inner experiencing and overt behavior; and for another, we sometimes formulate one side of the personality which requires the juxtaposition or superimposition of data obtained in the treatment history in order to bring out a meaningful three-dimensional picture. The psychologist and the therapist each hold one half of the coin in such cases, and no greater mistake can be made by the uninitiated than to assume at once that there is an irreconcilable difference in the findings, assuming, of course, that neither one nor the other has gone astray in his formulation of the case. If this assumption is correct, one must ask the right question, namely, "What is the meaning of the apparent discrepancy?" rather than conclude that someone has missed the boat.
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> With the asking of the proper question, one may find that the psychologist is bringing out conflict residuals no longer apparent in the patient's behavior and occupying a different temporal position in his life; or the psychiatrist's formulation may be based upon a flight into health, a successful reaction-formation, or a transference "cure". An understanding of the permutations and combinations involved in the examiner-tests-patient-therapist configuration can help solve many psychodiagnostic riddles.

While clinical validation of projective test findings is considered to be the ultimate validative criterion, some attending psychiatrists and residents are inclined to accept or reject a report upon the basis of whether or not it agrees with their clinical impression of the case. This test of instant congruence ignores a number of basic factors that govern the issue of congruence in general: The fact that crucial data relevant to a comprehensive understanding of the patient's psychodynamics are hard won over a period of time by the therapist, that they cannot be forced from the patient because of the latter's resistances which must be respected and which it is the therapist's task to help the patient overcome, and that data obtained under these conditions tend to be phenomenological and impressionistic. Furthermore the psychodiagnostician is often dealing with several levels of the patient's personality which he attempts to integrate. Less discernible levels explicated in the report often cannot be matched with a clinical referent because such referents are not yet available and must await their emergence in the therapeutic setting. Finally, there may be a misunderstanding of the psychologist's function by assuming that his function is to confirm the clinical impression on an all-or-none basis.

Actually, a more realistic conception of the psychologist's role as a diagnostician evolves over a time span during which misconceptions on both sides are ironed out. The confirmatory contribution of the psychologist's report is not to be underestimated in terms of its value to the resident's morale and as an independent assessment of his professional acumen during the training period. But, in addition, the report provides new information, enlarges the therapist's perspective on the patient's problems, transforms static clinical information into strategic material crucial to the therapeutic process, predicts some of the vicissitudes likely to be encountered in the transference relationship, suggests accessible payoff areas within the conflict configuration, and discusses the type of therapy most suitable for the patient in light of his personality and psychodynamics.

Research

Over the years the Division of Psychology has been involved in many projects, either on an individual basis or in collaboration with psychiatrists and allied professionals in such areas as the utilization of psychological tests (2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13), surgery (14, 15), prenatal clinic (16, 17), hyperbaric chamber (18), psychosomatic medicine (19, 20, 21, 22), obstetrics and gynecology (23), sexual identification and role (24), sexuality (25, 26), intellectual functioning of ethnic groups (27, 28), occupational therapy (29), interprofessional relationships (30), training of psychologists (31), and a comprehensive long-term evaluation of the impact of early psychiatric intervention upon the mental health and academic efficiency of disadvantaged primary school children (32).

The records of thousands of patients in our files, examined with full test batteries, provide an exceptional pool of data for future research on the reliability and validity of predictive parameters, the relationship between test-derived and discharge diagnosis, the relevance of psychodynamic delineation to the treatment process, changes in the incidence of certain psychiatric disorders over a span of more than two decades, and pinpointing of test data that have a direct bearing upon treatment planning. Computer services available in the hospital facilitate the research enterprise in this area.

Members of the division have, because of their specific training in research methodology, provided consultative services to residents and staff on research projects within the department. Too often what is regarded as research consists of clinical observations and impressions, which, even though systematized, tend to be essentially exploratory and should be used as the basis for hypothesis-development antecedent to the development of an experimental design within the framework of sound research methodology.

New directions in psychiatry and clinical psychology, especially those related to community mental health and the role of the Mount Sinai School of Medicine will undoubtedly bring about changes in professional roles and functions in the near future. These will require flexibility and readiness to experiment with innovative approaches to patient care. The cordial relationships enjoyed by psychologists in the Department of Psychiatry augurs well for the collaborative enterprise.

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Emergency Room Psychiatry: a Gateway to Community Medicine

LOUIS LINN, M.D.

General Considerations

During the past decade the utilization of hospital emergency rooms has increased at a rate exceeding by far that of all other hospital facilities. Patients of every age have come pouring into the emergency room (ER)—victims of physical and emotional stress for which a swift professional response may be a matter of life or death. In addition to this overall increase in the number of ER cases other trends have emerged. For example, in 1965, as a result primarily of a great increase in third party payments, the major caseload shifted from the municipal to the voluntary hospital ER. Most of the cases were children and young adults. In the older age group there was a preponderance of unmarried nonwhite males. The role of social and family disorganization was suggested by the high rate of ER patients who came from the lowest socioeconomic stratum in which the head of the household was absent or unemployed (1).

Most ER patients come from families without a regular family doctor. Many of them are in need of immediate care but their problems are not the life or death issues for which one ordinarily reserves the term "medical emergency." These are the patients for whom the family doctor once upon a time made house calls or saw in his office without a scheduled appointment. With the trend toward specialization and the disappearance of the general practitioner this new pattern of ER medicine appeared, first among the socially disadvantaged and then increasingly among patients from all social classes. It is not uncommon for a physician to rendezvous in the ER with his private patient for a minor surgical procedure or for diagnostic evaluation of an acute medical or surgical condition. Whereas Blue Cross will not reimburse a private physician for procedures in his office, it will often do so if they are carried out in the ER, particularly within 24 hours after accidental injury. This payment pattern tended to funnel all patients into the ERs of voluntary hospitals, regardless of social class.

Thus, the ER is on the way to becoming the *one door* to the community health care system (2). Like Janus, the two-faced Roman god of doors, the ER faces both the outside community and the community within the hospital. These separate communities converge on the ER. Individuals seek help on their own. Others are directed there by private physicians. Schools, social agencies, and the police also refer patients to the ER. As the receiving center for the community the ER becomes a logical point for "triage." Triage is the process of placing patients in the most appropriate treatment channel. It may include acute care in the ER, more complicated procedures in daycare beds, overnight care in the ER area, admission to regular inpatient beds, referral to outpatient clinics and social service, or to specialized hospitals, clinics and social agencies elsewhere in the community.

An ideal ER system strives for continuity of care. It focuses on the total patient and his family as well as the total community in which the family lives. To the extent that ER medicine concerns itself with primary prevention it will have to utilize social agencies to fulfill a broad health, education, and welfare mission for the surrounding community. In short, the ER can become, one day, the key element in a comprehensive community medicine program.

Before this can be achieved, however, certain paradoxes of ER medical practice must be resolved: 1) Although most patients treated in a hospital establish their first contact with the hospital through its ER, only a tiny proportion of hospital space is allocated to it. At Mount Sinai, for example, 70 percent of all patients pass through the ER annually, and yet the latter occupies only 1 percent of the total hospital area; 2) In terms of personnel, the ER represents an even smaller percentage of the total hospital staff; 3) Most important, professional competence in the ER is probably lower than at any other point in the hospital. Typically, the ER is staffed by interns at the earliest stages of their postmedical school training. Back-up care is given by residents on call. Attending physicians are nominally available for ER consultation but are in fact rarely consulted.

Only after these problems are solved can the ER become a door through which anyone may pass, with any complaint, at any hour of the day or night, and receive prompt, courteous and competent care. But first the voluntary hospitals need a fundamental revision in their point of view concerning community obligations. Even more, they need administrative revisions to give the ER the chance to function as a separate hospital department with a top flight staff of its own, a program of its own and a budget of its own.

That the issues of ER medicine are reaching a critical stage is suggested by the formation of the American College of Emergency Physicians (ACEP) in August of 1968. This is a legally constituted society of licensed physicians dedicated to the improvement of emergency services. The goals of ACEP have been set forth as follows: 1) Establish standards of ER care; 2) Provide training and continuing education for ER physicians; 3) Study the socioeconomic aspects of ER medicine; 4) Educate the general public about primary prevention and the most effective use of ER services; 5) Promote research to improve ER care; 6) Facilitate communication within the ER staff and with the rest of the medical community; 7) Establish a working relationship between the ER and the private practitioner.

Although recognizing that it is as yet without credentials as a separate specialty, it is the hope of the organizers of ACEP to present evidence in the literature and in regular scientific meetings that quality training and experience in ER medicine are sufficiently distinctive to merit this new academic category.

Psychiatric Considerations

Having presented these general considerations concerning the ER, we will now turn to ER psychiatry, with particular reference to our experiences at The Mount Sinai Hospital. In a presentation in 1969, Bernstein, Straker, and Childs (3) characterized the situation as follows: "The ER facility for psychiatry is presently located in a small office adjacent to the adult ER. Patients requesting to see a psychiatrist or those referred by the ER staff are required to wait in the general ER waiting area which resembles a crowded bus depot. There are no nurses in the area specifically trained in psychiatry, no facilities for handling a disturbed patient, and no beds specifically allocated for psychiatry. It should also be pointed out that there is no staff specifically responsible for psychiatric patients and often two to three hours may go by before they are seen [and then] by [an inexperienced] psychiatric resident and some leave before being seen. The clerk at the registration desk is usually the person determining whether a psychiatrist is called either upon request of the patient or for obvious nervousness. These patients are seen by the [first-year] resident on call who is assigned for that particular day [both] to the ER and to his own inpatient unit. He is available for 24 hours and has access to the chief resident on call for consultation concerning difficult dispositional problems, especially those cases requiring hospital admission. It should also be pointed out that the ER functions in isolation from the rest of the department of psychiatry. Indeed, it is the only psychiatric facility connected with the hospital in which there is absolutely no teaching supervision." Under these circumstances it is not surprising that psychiatric patients were grossly underrepresented in the overall ER census (and this was particularly true in relation to our own catchment area), and that communication between psychiatric and other residents was at a minimum as expressed, among other things, by the fact that less than 10 percent of all the psychiatric cases were referred by the ER staff.

To complete this dismal picture it should be added that nowhere in the hospital are the psychiatric problems as complicated as those encountered in the ER. On the wards and in the clinics, cases are carefully selected for motivation and psychological accessibility. In the ER we see in unselected array all diagnostic categories and all degrees of severity of illness.

In no other clinical situation is speed in the decision-making process so essential. Whereas the young resident has weeks and even months to reason out an ideal disposition for an inpatient or the best treatment approach for a clinic patient, in the ER time for deciding is usually measured in minutes. Furthermore, the triage problems, that is, the number and variety of dispositions, are more complex in the ER than at any other point in the hospital's mental health care system (14).

All things considered, it is easy to understand why the beginner's first reaction to ER duty is apt to be one of phobic avoidance manifested by long delays in responding to calls, by resentment, and by bitter complaints.

It must not be supposed that this is a situation peculiar to The Mount Sinai Hospital. On the contrary, it is a universal problem and has been well described by Beahan et al in relation to what they call the "uptight ER resident" (5).

The Reorganized ER

The plan adopted at Mount Sinai Hospital in July of 1969 was a simple one. If the psychiatric problems in the ER are indeed maximally complex, why not station psychiatrists there who are maximally qualified? It was our idea to staff the ER with attending physicians who would be physically present in the ER on a regular basis during daytime hours. Since no funds were available for this experiment we had to recruit psychiatrists from our voluntary attending staff who were willing to accept assignment in the ER in addition to, or instead of, other department obligations. In a short time several attending psychiatrists rallied to the cause. What made the project truly operational, however, were the contributions of Dr. Cervando Martinez, a third-year resident, who understood at once the implications and potentialities of the project. Not only did he volunteer for all sessions not yet covered by attendings, but he participated in our early deliberations with maturity and creativity.

Our next step was to establish a working relationship with the Department of Community Medicine. In September of 1969 we met with Dr. Jane Moss, sociologist, and Mrs. Renate Belville, research assistant, both from Community Medicine. Together we developed a standard ER evaluation interview to facilitate a swift but thorough work-up. By thus systematizing data collection we expected not only to improve the quality of care but also to lay the foundation for evaluation and other aspects of clinical research (6).

While we encountered many patients who were emergencies in the traditional sense that they were dangerous to themselves or to others, we operated in accordance with the broader concept that there are emergency moments in the course of almost any illness when immediate and intensive intervention may yield dramatic improvements and prevent long-term chronic disability (7).

Accordingly, we formulated our goals (8):

1) Establish a close working relationship with the nonpsychiatric ER staff. We are in the process of equipping our ER psychiatric attendings with white coats and identifying badges to emphasize that they are part of the larger ER team.
2) Reduce or eliminate long delays for patients, thereby reducing frustration or resistance both on the part of the staff and the patients.
3) Provide a walk-in clinic in the ER so that patients could be seen repeatedly for evaluation and/or treatment, the latter to consist of short psychotherapy sessions, supportive in nature, supplemented with medication as needed, and available in the ER electively or by appointment.
4) Provide more experienced physicians to do a more comprehensive initial interview so that more appropriate dispositions would result. Among other things we hoped to reduce the need for long-term full-time beds.
5) Provide treatment and reevaluation for patients on waiting lists.
6) Avoid the office practice model of waiting for patients to come to us. By making rounds in the ER, by establishing the presence of a "floating" ER psychiatrist, we hoped to find cases that would otherwise be missed.
7) Provide psychiatric teaching to personnel at all echelons of training.
8) Develop a program of clinical research.

Results

During our first few months certain facts emerged:

1) There has been an appreciable increase in the number of psychiatric cases seen. This is a consequence of referrals from several sources, as follows: (a) From our ER staff, doctors and nurses. The referral rate from this

source jumped from seven percent to 14 percent of the total in the first three months of operation. Since the majority of patients seen in the medical and surgical ER are from our catchment area this has produced an increase in the number of psychiatric visits from our catchment area from 17 percent to 25 percent. Several patients were seen in whom a physical diagnosis concealed an underlying psychiatric disorder and vice versa.

As the referral rate from this source went up the self-referral rate dropped comparatively. Typically, self-referred patients are brought in by family or friends. Few community isolates come in on their own; this suggests the need for some type of "reach-out" program.

(b) The Social Service Department has become an increasingly important source of referrals. For instance, patients discharged from a surgical service without providing necessary OPD psychiatric follow-up care have been properly channeled by means of an ER referral.

(c) There has been an increase in revisits both on a walk-in basis and by appointment. It has been instructive to observe a distinct rise in the percentage of kept appointments. It seems irrelevant to speak of poor motivation in the ghetto patient or of a supposed culturally determined unconcern for scheduled appointments when the only solace offered is a screening interview of uncertain outcome several weeks after the crisis. If we give more, patients are prepared to cooperate more. Of even greater significance is the fact that an elective return appointment is decidedly more effective than a fixed appointment in maintaining a working relationship with ER patients.

(d) Agencies in the surrounding community have begun using our ER facility increasingly. We developed a particularly close relationship with the Little Sisters of the Assumption, a nursing order that provides a broad range of services to the East Harlem community (9). We see patients whom the Little Sisters bring to the ER. We also assist them consultatively in weekly case conferences. They, in turn, are prepared to make home visits at our request in relation to ER cases from our community.

(e) Various hospital employees have been sent to the ER by their supervisors.

(f) Other clinics in the hospital, for example, the methadone clinic or the diabetes clinic have referred psychiatric patients to the ER.

(g) As physicians in private practice become aware of the presence of psychiatric attendings in the ER we expect an increasing number of referrals from the private practice sector.

(h) Because the ER caseload is much heavier in the afternoon hours we are urging that all elective ER referrals be directed to morning sessions.

By distributing an ER duty roster it has become possible to refer a patient to a specific attending psychiatrist in the ER. The psychological advantage of this requires no elaboration.

2) We have run a consistent female over male ratio of three to two. On one hand, this reflects a hospital-wide ratio. It also reflects that we do not have an ambulance service, a fact which eliminates many cases brought to the ER with physical injuries incurred by accident, assault, or self-infliction. As a result male patients are considerably underrepresented in our hospital population. In any event, one must conclude that under stress the male patient breaks down along different diagnostic lines. This is not difficult to demonstrate. For example, in our own methadone clinic (for the treatment of heroin addiction) the female/male ratio is 1/15. A study of adolescent ER visits in New York City has shown that half the cases have been victims of some form of accident or violence, most notably among males 15 to 24 years of age. In this age group homicide and suicide now account for more than two-thirds of all deaths (10). It is our hypothesis that common factors are at work causing male patients to break down in one way and female patients in another and that the ER is the final common path for both. In accordance with this hypothesis, it is important that all ER patients (psychiatric and nonpsychiatric alike) be studied together and treated together (11).
3) A preliminary survey of patients sent from our ER to municipal hospitals for inpatient care reveals that the majority are back in the community within three days. This finding emphasizes the need for a short-term inpatient emergency treatment unit (ETU). Weisman and his group at Yale (12) found that fully 82 percent of the patients admitted to their ETU could be returned to the community within three days. A one-year follow-up showed that fully three-fourths of these cases were still functioning in an ambulatory setting. At this time one can only surmise the saving to the entire community that this represents, not alone in terms of money, professional time and effort, but also human welfare in terms of families kept together and regression prevented.
4) The ER as an ideal setting for psychiatric teaching was summarized for us by Lothane (13):
    (a) Certain acute phases of illness, psychiatric or otherwise, can be seen only in the ER and may actually disappear en route to the ward. This can occur, for example, in relation to major hysterical attacks which may not manifest themselves in the sheltered setting of an inpatient service.
    (b) Because ER patients are usually accompanied by key relatives or friends there is an unexcelled opportunity to learn firsthand about the patient's interactions with his family and the social setting of his illness.
    (c) The ER is a crossroad where the patient and the various community agencies intersect (welfare, social work, law enforcement), as well as other agencies and clinics of the hospital. Here is the ideal place to see the interdisciplinary team in action.
    (d) The ER is the place to develop skills in triage, rapid and accurate clinical assessment, crisis treatment and follow-up care.

The leisurely pace of an inpatient service, the modifications of the acute clinical picture as a result of separation from a traumatic environment, and the support of a sheltered inpatient setting (protective of both physician and patient alike) make for a highly unrealistic picture of the clinical course of mental disorder. Instant relapse is the usual fate of improved inpatients discharged to an inimproved home environment.

The tendency to glamorize and overemphasize the technology of inpatient treatment leaves medical trainees at all echelons of responsibility unprepared for the pragmatic realities of ambulatory care in the ER. For the medical student this can be remedied only by a carefully supervised ER clerkship. We have to achieve this for the nonpsychiatric house staff by maintaining the physical presence of the "floating" psychiatrist in the ER who also encourages a consistent psychosomatic point of view. In addition the ER attending has an opportunity to teach in the monthly orientation conferences for new interns and social workers.

The ER attending psychiatrists are available to our psychiatric residents electively for consultations and supervision. In addition there are weekly ER conferences to which ER residents are invited to bring up cases with which they want help. The ER nurses have been particularly responsive to educational opportunities offered by the ER attending psychiatrists. Conferences have been conducted with nurses, focusing not only on problem patients but on staff morale as well.

Staff morale in the ER is a most important issue. Dr. Martinez has characterized the daily uninterrupted responsibilities of ER duty as "a very exhausting, frustrating, and agonizing experience." In his opinion, residents should not be assigned to the ER prior to their third year of training and then for a period limited to three months. The resident on ER duty may be likened to a rifleman in combat. He needs extra time off and perhaps extra pay. What he needs most of all is careful supervision by senior attendings who will not only ease the heavy pressure of ER duty but make this experience a maximally rich opportunity for learning.

Special Issues

Social Services

We asked our Social Service Department to prepare a memorandum suggesting how they could help in the ER. The following was submitted (14): ". . . Social Service can assist either by providing direct service to the patient or, if indicated, by referral to appropriate community agencies, depending on the individual situation.

1) GENERAL SERVICES
   (a) Financial assistance
   (b) Problems with Department of Social Service
   (c) Housing (and sanitation problems)
   (d) Home management problems

  - (e) Child care and/or management problems
  - (f) Employment and vocational guidance
  - (g) Legal Aid referral
  - (h) Acute and/or emergency environmental problems
  - (i) Certain types of personal adjustment problems
  - (j) Family relationship problems
  - (k) Marital problems
  - (l) Nursing home and chronic care planning

2) CHILDRENS' SERVICES
  - (a) School adjustment problems (including learning and or behavior)
  - (b) Special planning for the handicapped child (physical or emotional)
  - (c) Special placement services
  - (d) Day care or camp
  - (e) Family–child relationship problems

3) SERVICES FOR THE AGED
  - (a) Problems of housing and residence
  - (b) Assistance in nursing home and home care planning
  - (c) Referral for recreational or vocational facilities
  - (d) Problems of social adjustment-social change
  - (e) Problems of family relationships."

In the light of this impressive list it is regrettable that so far there is not a single social worker with a direct assignment to the adult ER. However, individual workers from separate services have consulted with ER attendings concerning special dispositional problems. In addition, the Social Service Department is preparing a plan of its own to promote more effective use of social workers in the ER.

The Violent Patient

Aggressive behavior in mental illness is relatively rare. The fear with which some people regard all psychiatric patients is completely out of proportion to the rather small group capable of inflicting harm on others (15, 16). One does not require a special clinical approach for the latter. As in any case an attitude of calm and objectivity is indicated. If one takes enough time for a proper history, it will be found that there are many types of disturbed behavior, each requiring its own treatment. For example, a personality type has been described by Lion and co-workers (17) with a characteristic history of family disorganization, punitive parental violence in early childhood, enuresis, firesetting, cruelty to animals, and polymorphous-perverse sexual behavior in adult life. These patients have a low frustration tolerance and react violently when crossed. Although violence is usually directed against family members, it may be expressed indiscriminately during periods of acute stress. Such people often come to the ER voluntarily, asking for help because of impending loss of control. Needless to say, one should not add to their frustrations by prolonged waiting in the ER and red tape. "Patient advocates," or ombudsmen, are individuals specially trained to intercede for bewildered patients in relation to the hospital bureaucracy (18).

As paid indigenous nonprofessionals or as volunteers they are currently being used at The Mount Sinai Hospital to meet this need. An effective response represents important protection to society. Thus, the violence-prevention role of the ER is not less important than that in relation to suicide.

Transient situational disturbances in all age groups may result in tantrum-like outbursts requiring crisis therapy. Assaultive reactions to alcohol, particularly during the dissociative states characteristic of pathological intoxication, are common and dangerous. Toxic substances other than alcohol, such as methedrine, cocaine, and LSD, may precipitate psychotic reactions associated with violence. Metabolic and circulatory disturbances may show up clinically with delirium.

Occasionally assaultive behavior is a manifestation of epilepsy and we have referred ER cases to Dr. Seymour Rosenblatt who is studying this problem. And, of course, assaultive behavior is seen from time to time in schizophrenic and manic-depressive psychotic states. Concerning these, Barton (19) has said: "A frightened but docile person who is accosted in a hostile and aggressive manner can be turned into a barricaded battler. But the reverse is equally true. Most disturbed people who are already standing their ground and making threats can be quickly rendered cooperative by someone who is trained and who knows what he is doing. It is mainly a matter of bringing in a staff person well experienced in dealing with patients who can give a show of confidence and transmit the expectation that the patient will behave well. If threatening patients were invariably handled this way, very few of them would have to be brought to hospitals by force."

Disturbed psychotic patients will often accept hospitalization if personally escorted to the hospital by the referring physician who stays with him until the admission procedure has been completed. Once an attitude of trust has been achieved, many disturbed patients will cooperate for the administration of rapidly acting parenteral tranquilizing medications. Only rarely is it necessary to resort to physical restraint in order to control disturbed patients.

The Suicidal Patient

The ER plays a paramount role as a suicide prevention center. As in the management of the assaultive patient, a swift sympathetic response is essential. The administration of antidepressant medications and the offer of a return visit to the ER is often enough to tip the clinical balance against suicidal acting-out. Suicidal patients are the ones who most frequently need short-term inpatient treatment in an acute care unit. We encourage emotionally fragile patients to maintain telephone contact with the ER attending via our special extension.

Crisis Therapy

Most ER patients have a lifelong history of psychopathology, often severe, in spite of which they have managed to adapt. These people seek ER help only when this adaptational mechanism has decompensated. Usually the breakdown results not so much from a change in the patient as a change in others. A parent, a spouse, other key relatives, an employer, a teacher, etc., may have finally experienced an exhaustion of patience and hope. Silberstein (20) has characterized this situation as one in which the patient's "reservoir of social credit" has become exhausted. A prompt response in the ER, a vigorous treatment program in an outpatient setting and supportive environmental change with the aid of social service, can restore the patient's "social credit" and may delay or even obviate the need for inpatient care. This pattern of care, one which depends on the immediate availability of a treatment team which addresses itself specifically to the current situation responsible for the breakdown, is what we mean by "crisis therapy." It is an approach too frequently neglected in training facilities and it can best be met by an effective ER program.

Research

The ER service is the mental health facility in the community which is "least selective and restrictive and most readily available. By its very nature it is ideally suited to detect early and subtle changes in the symptomatic and demographic characteristics of the population at risk" (21). This makes the ER an ideal focal point for community mental health research. Our plan to collect data systematically for periodic evaluation is currently our major research effort. We are in the process of developing other projects. For example, we are developing a family-centered approach to post-heroin-injection hepatitis victims. A similar study is planned for status asthmaticus. We also plan to explore the role of the hospital's Consultation Clinic in relation to the ER population.

Future Plans

1) The most urgent item on our agenda is to systematize the voluntary attending staff's schedule. We should have two attendings for each session not only because the service and teaching load warrants this but because when only one attending is on duty his unavoidable or enforced absence can be most disruptive. We would like to see all newly appointed attendings serve in the ER for a year or more before going on to other assignments. In addition to this expanded voluntary staff we should have one full-time or two half-time paid attendings to coordinate the ER program.

OPD Liaison Psychiatry currently operates on a low level of efficiency. Often an attending arrives at the assigned clinic only to find no consultations waiting for him. In time he may take to telephoning the clinic to determine in advance if there are cases waiting and if there are none he may not appear at all. We believe that the situation could be improved by assigning each OPD Liaison Psychiatrist to the ER as his primary assignment and to his specialty clinic as his secondary assignment. This would increase ER manpower and increase the efficiency with which we use the time of these highly experienced attendings.

2) If funds become available we would like to staff the ER with paid psychiatrists every night from five to ten o'clock and during the daytime hours on weekends. In addition we would like to see a strong ER staff of paid social workers, case aides, indigenous non-professionals, as well as a staff of volunteer workers specifically trained for ER service.

3) Currently there are separate attendings in charge of ER medicine, ER surgery, ER pediatrics and ER psychiatry. Thus far interactions between them have been slight. We hope to institute regular meetings of these four attendings under a common umbrella to develop an overall ER program which will be family-centered, with a community base and an health-education-welfare focus, with comprehensive services and continuity of care for all; in short, an ER approach that could be the foundation for a broadly based Community Medicine program.

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The Individual Therapy Clinic

A Community Service and a Learning Experience

HANS J. KLEINSCHMIDT, M.D.

Shortly before the end of the First World War in 1918, Freud addressed the Fifth International Psychoanalytical Congress convened in Budapest. Hopeful that psychoanalysis would not be reserved to an affluent minority, with characteristic forethought, Freud remarked that "...it is possible to foresee that at some time or other the conscience of society will awake and remind it that the poor man should have just as much right to assistance for his mind as he now has to the life-saving help offered by surgery; and that the neuroses threaten public health no less than tuberculosis, and can be left as little as the latter to the impotent care of individual members of the community. When this happens, institutions or outpatient clinics will be started, to which analytically trained physicians will be appointed, so that men who would otherwise give way to drink, women who have nearly succumbed under their burden of privations, children for whom there is no choice but between running wild or neurosis, may be made capable, by analysis, of resistance and of efficient work. Such treatments will be free. It may be a long time before the State comes to see these duties as urgent. Present conditions may delay its arrival even longer. Probably these institutions will first be started by private charity. Some time or other, however, it must come to this. We shall then be faced by the task of adapting our technique to the new conditions"(1).

The recognition of the human cost of neuroses to society has been a gradual historical development over the past fifty years. Freud's concern for the future becomes prophetic, when one realizes that there is hardly a general hospital today without a psychiatric therapy clinic. In 1970, there were approximately 500 psychiatric outpatient services available to the public in the United States alone.

The adaptation of technique, which Freud anticipated, has also occurred. Instead of classic psychoanalysis, clinic patients receive psychoanalytically oriented brief psychotherapy. Such an adaptation of technique is not necessarily a compromise, for as it has been demonstrated, many patients are not suitable candidates for analysis. Many patients, too, come to the clinic because of a specific crisis situation, and in such instances, a less comprehensive historical approach is indicated.

As an adaptive method, psychoanalytically oriented psychotherapy demands equal skill and knowledge from the therapist. While concentrating on the patient's present life situation, the therapist, at the same time, must reconstruct the psychological meaning of the patient's past and bring this composite perspective to focus in therapy. Such a skill demands a thorough understanding of psychoanalytic principles and an assimilated awareness of various techniques.

The Adult Individual Therapy Clinic at Mount Sinai Hospital provides psychoanalytically oriented psychotherapy to anyone who requests a screening interview, as well as to patients referred from other departments of the general hospital. To insure the right of the poor to treatment, the only restriction placed on the right to treatment by the hospital is proof of lack of financial means on the part of the patient. The clinic fee is a nominal one.

During the year 1969, approximately 260 patients were treated by our second- and third-year residents. The following table is a breakdown of the patient population in the Adult Individual Psychotherapy Clinic in the years 1966 through 1969.

PATIENT POPULATION IN THE ADULT INDIVIDUAL PSYCHOTHERAPY CLINIC

	1966	*1967*	*1968*	*1969*
Census, January 1	96	92	143	149
Admissions	34	88	111	115
Readmissions		1	1	2
Closings	38	38	106	80
Census, December 31	92	143	149	186
Total Cases Treated	130	181	255	266

Each resident carries a caseload of between five and seven patients. After a first screening session, the resident reviews the case with an attending and discusses the suitability of the patient for ambulatory psychotherapy versus admission to the Day and Night Center, the Inpatient Service or any other disposition deemed advisable. The resident also meets with a preceptor at least once a week to discuss in detail the therapeutic process with respect to each patient. In addition, he has the opportunity to consult with the chief of the clinic at any time to discuss an acute crisis or new disposition.

As part of the nonresidential hospital services, the Individual Therapy Clinic makes an important contribution to the community. At the same time, it provides an extremely vital learning experience for our second- and third-year residents. It is a challenging and most difficult task to reconcile our responsibility toward the community we serve with the increasing demands for "relevant" and "meaningful" training through supervised work with "interesting" patients on the part of our residents.

Several years ago, a group of second-year residents requested that more time be given to supervised work in the Outpatient Department. The residents justified this request on the basis that clinic experience was the closest approximation to their future practice in psychiatry, and hence with more experience in treating clinic patients, they would be better prepared. In addition, a further justification has developed recently because no longer does outside financial assistance permit extended periods of inpatient treatment.

The average stay of inpatients on any one of our hospital units has decreased so drastically that a thorough study of the psychodynamics involved and of the interaction in the psychotherapeutic process becomes a pious wish rather than a feasible undertaking. Three weeks are not nearly enough to allow the experience of those subtle nuances in the doctor–patient relationship which come about in time. But with rising hospital costs, "time" becomes a rare commodity on the Inpatient Service.

Traditionally, in most hospitals, the hierarchal structure has centered around the Inpatient Service. Indeed, it can be said that the Outpatient Department has been treated as psychiatry's step-child. Because of the farsightedness and flexibility of Dr. Kaufman, a rigid adherence to hierarchal structure has been avoided, and the resident training program at Mount Sinai has become most responsive to the needs of the residents. Meeting the residents' request for more outpatient clinic experience might have led to an intense rivalry between inpatient and outpatient faculties, but the leadership of Dr. Kaufman bypassed this hazard, and, instead, brought with it an exciting expansion of learning and teaching possibilities for residents and faculty.

Mount Sinai has been most fortunate in its selection of psychiatric residents, for the added hours spent in the Outpatient Department requires an unusual willingness for hard work and a keen sense of personal responsibility. At the present time, second-year residents participate in the program of the Individual Therapy Clinic for eight hours a week. These eight hours, however, do not include time spent in the Aftercare Clinic, the Emergency Care setting, or the Suicide Prevention Clinic. Each resident is assigned a preceptor and is expected to attend two clinic case conferences every week.

Our clinic conferences serve as important learning experiences. Tuesdays are reserved for formal case presentations and discussions of psychodynamics, clinical diagnosis, therapeutic goals, and strategy. The Friday conferences are devoted to a more intricate examination of the approaches and techniques in therapy with the very same patient presented by the resident at the Tuesday conference. The residents are thus given the opportunity to look at themselves candidly and honestly as therapists and to ventilate their self-doubts and insecurities. The use of taped sessions for these conferences has also been found helpful.

There is little doubt that today's resident views his responsibility to himself as well as to his society differently from his older colleagues. The social urgency of the present time makes it understandable that the young resident psychiatrist wants to reach a larger and more varied group of people than his predecessor. Although the returning veterans after the Second World War made the psychiatric profession aware of its increasing responsibilities to the community, there is no precedent for the recent clamor for storefront psychiatry, walk-in clinics, drug abuse programs, and emergency crisis services.

Man's dream that technology would somehow lessen his burden, if only to permit him more time for reflection, has simply not been realized. A significant difference between the resident of the forties and the resident of the seventies is that the present-day resident has so much less time for private reading, reflection, and assimilation of experience.

Our field abounds in information today. Understanding, however, requires a systematic and analytic approach. The basis of all scientific thought or any systematized approach to knowledge is the analytic method which Freud was the first to apply to psychological problems. One difficulty in instilling the analytic method in psychiatric residents today is their mistaken belief that the analytic method is to be equated with a purely Freudian orientation. How difficult it is at times to convince the young resident that there is no scientific method without a systematic approach; and that there is no systematic approach without an analytic framework!

If sound independent thinking is to be the ultimate goal of education, then familiarity with the history and development of ideas is essential. But one finds too often among the residents proponents of behavior therapy who are completely ignorant of the fact that behaviorism was popularized in the twenties by Watson. Although the controversy surrounding behaviorism today is very reminiscent of the dispute which occurred nearly 50 years ago among the critics of Watson, many residents are simply disinterested in such historicity.

It has become a commonplace that the students of today are antihistorical. But the unknown can enslave just as certainly as the ballast of history. There is a readiness among the young to disregard the historical development of ideas, although it should be emphasized that there is no homogeneity in student groups, or, for that matter, in any group. But the issue today is not between a Freudian or non-Freudian approach, but between those who adhere to a historio-analytic method and those who would recognize only unsystematized empirical observations.

We try to convince our residents that the danger of accepting enthusiastically what might well be impressive therapeutic results without an analytic understanding of those results and of the theory implicit in the application of any particular psychotherapeutic technique, is that such an uncritical acceptance can lead to an unwittingly harmful experimental attitude toward patients. And experience would indicate that teaching is most effective when a specific point of view is maintained. Such a point of view does not necessarily imply an uncritical acceptance but is used mainly as a frame of reference. For example, if we were to expose our students to the multitude of available psychotherapeutic techniques and schools of psychiatric thought without a frame of reference, we would simply be presenting information without education, and at the same time deceiving ourselves into believing that education can be value-free.

Far from immobilizing original thinking, profound familiarity with what might be presently viewed as closed systems of thought, surprisingly can often provide the springboard for a departure into new channels of scientific pursuit. The well-known example of Johannes Müller and Helmholtz comes to mind.

Johannes Müller, the eminent nineteenth century physiologist, was the teacher of Brücke (in whose physiological institute Freud worked for six years), Du Bois-Reymond and Helmholtz. Their boundless admiration for their illustrious teacher did not inhibit their efforts to prove vitalism, Müller's fundamental belief, wrong. According to the vitalist doctrine, "a rational creative force is exerted in every animal strictly in harmony with what is required by the nature of each"(2); this mysterious vital force is eventually used up and dissipated. Müller seemed convinced that physics and chemistry could never fully explain the processes of life. But in 1842, Brücke and Du Bois-Reymond declared, "No other forces than the common physical chemical ones are active within the organism." And in 1847, Helmholtz established the principle of conservation and transformation of energy.

Johannes Müller had asserted that it would never be possible to measure the speed of transmission of the nerve impulse. But experiments conducted by Du Bois-Reymond led Helmholtz to assume that it might be possible by relatively simple means to accomplish this feat. When Helmholtz succeeded in measuring it, his teacher congratulated him on his spectacular achievement, defended him against scientists who at first doubted the validity of the experiment, and insisted on publishing the findings in *Müller's Archiv,* his own prestigious archives of physiology. Dogmatic adherence to outmoded theories and doctrines was so alien to him that he did not mind to be proven wrong by his own students and actually made no secret of his pride in their scientific achievements (3).

It is in the same tradition that Dr. Kaufman has succeeded in all sections of the department to bring about a balance between a definite psychoanalytic orientation and a genuine interest in new ideas, approaches, and assessments. This has imbued the faculty with a spirit of intellectual responsibility, a challenge to rethink conclusions reached earlier, and a climate free from dogmatism. The interplay between faculty and students has probably been largely responsible for the department's adaptability in meeting the needs of the community.

In the clinic the resident is confronted by patients with the widest possible variety of educational as well as socioeconomic backgrounds, presenting a marked diversity of problems. He soon learns that it is an inherent part of a sound professional attitude as psychiatrist and physician to treat people in need of help whose problems present no intellectual challenge, whose personalities are not always likable, and whose educational level is quite low.

That there is good reason for the policy of assigning patients to each individual resident rather than to leave the choice of patient to the resident is best illustrated by the findings of Hollingshead and Redlich at Yale (4). Patients of some standing in the community with fair to good educational background received psychotherapy, while those less fortunate with whom the therapists were unable to establish ready rapport, were treated with drugs or referred for shock treatment. The Hollingshead-Redlich study underscored the importance of step-by-step supervision of residents from the assignment of patients to the planning of a course of treatment based on unprejudiced evaluations but at the same time on realistic goals.

Looking over the past ten years, the first thing one notices is that we treat far more patients in our clinic, and thereby serve the community more effectively. Our desire to meet community needs has in no way meant a compromise of standards. Mount Sinai has so far been successful in benefiting from new developments, including technology, rather than succumbing to the dehumanizing influence of the computer age.

Undoubtedly, computer psychiatry and other technological advances will come to our department at some time in the future. Such radical innovations need not disrupt the theoretical framework underlying our program to which Dr. Kaufman has contributed so greatly as educator and administrator. In the final analysis, it will be his humanist philosophy which will best safeguard the high standards of accomplishment, integrity, and dedication in every unit of the department.

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Aftercare

SAMUEL L. SAFIRSTEIN, M.D.

Twenty-five years may not be a long time as far as history is concerned, but it is often the greater part of a man's professional life. In psychiatry, with its prolonged training period, a quarter of a century of uninterrupted leadership in a concentrated area is a rare phenomenon. Dr. M. Ralph Kaufman had the foresight and ability to pioneer in the new field of psychiatry in a general hospital where his contributions have been outstanding. It is my pleasant task to discuss aftercare—the care of former hospital inpatients—as it grew, developed, and changed under his influence as Director of the Department of Psychiatry at The Mount Sinai Hospital of New York.

The importance assigned to aftercare was apparent when a separate Aftercare Clinic was opened at the same time as the inpatient unit in 1946. Heuristic and training aspects of aftercare were thus underscored, and a weekly conference conducted by Dr. Kaufman himself has emphasized its value. Today the Aftercare Clinic is the largest clinic in the Department of Psychiatry and at any time has a census of about 400 patients. In 1969, 576 patients were treated in the clinic; there were 205 admissions, 186 closings, and 15 readmissions. The staff consists of about 20 first- and second-year residents who provide the bulk of therapy and nine members of the attending staff who provide supervision, administration, and consultation. The clinic operates during two afternoons and one evening weekly. The services of a caseworker and a psychologist are available. Most of casework therapy with relatives of patients is done by caseworkers from the inpatient services. As with the psychiatric resident, continuity of service by the caseworker is preserved. The supervisory system is noteworthy in view of its importance both as a basic tool of resident training and as a major factor influencing patient care. The preceptors, who are attending psychiatrists, are an integral part of the Aftercare Clinic and are aftercare-trained and -oriented. The fact that aftercare is their only assignment and that they have been with the clinic for a number of years makes for cohesive functioning and enhanced effectiveness. In addition to weekly sessions with the chief of the clinic, meetings of the entire supervisory staff are held twice yearly during which matters of policy are reviewed and new ideas are discussed.

Looking back on the 25 years of functioning of the Aftercare Clinic, the most striking change appeared at first glance to have been the result of the opening of the Institute of Psychiatry at the end of 1962. This coincided with a considerable increase in psychiatric beds (from 22 to 110), and, not long thereafter, to the opening of a Day and Night Center for partial hospitalization. What this meant in terms of aftercare was a great increase of patients (from about 35 to the present 400) with the consequent need to train new preceptors. When the dust settled, however, our functioning continued very much as before, although on an enlarged scale, with the same principles of treatment and care prevailing.

The "open-ended" character of aftercare was one of those early principles; by this was meant that once a patient had been admitted to the Aftercare Clinic, he continued to be eligible for care and treatment for as long and as often as he needed it. By separating aftercare from other nonresidential services, special characteristics of the former were recognized, especially those which indicate its close affinity with residential services. This gave substance to the principle of continuity of both inpatient and outpatient services. The chief of the Aftercare Clinic has been in charge of administration, training, and research, and is directly responsible to the Director of the Department of Psychiatry (1, 2, 3, 4, 5, 6).

The importance assigned to aftercare for mental hospital patients grew in the course of years, as lengthy hospitalization and protracted custodial care were better understood not only in terms of their beneficial effects but also in terms of their possible disadvantages. Parallel with the trend away from long hospitalization, aftercare acquired an increasing meaningfulness and importance. Nowadays it is generally agreed that no inpatient services should exist without aftercare. At the same time any aftercare service in the community needs the "back-up" of an available inpatient department for possible hospital readmission.

It was only a matter of time before it was learned that aftercare can fulfill many functions (7). The foremost is that it can maintain a patient in the community, which is naturally of great advantage to the mental hospitals. Moreover, effective aftercare service can provide the patient with the benefit of living with his family, in his own milieu, partly or fully employed, and at much less cost than hospitalization. Whenever judicious and reliable aftercare is available, patients can be discharged from the hospital relatively sooner, and often before the condition of hospitalism has had a chance to set in; they can stay out longer between hospitalizations and perhaps can avoid rehospitalization altogether.

The same factors operate in terms of a psychiatric department in a general hospital where hospitalization is usually of much shorter duration. Dealing mostly with acute episodes of mental illness, the inpatient unit may choose to discharge its patients relatively early, namely, as soon as the acute episode is over, and leave convalescence, readjustment, and rehabilitation to ambulatory aftercare. (Indeed, early discharge may no longer be a matter of choice as governmental funds and third-party payments usually do not provide for more than a brief psychiatric hospitalization.)

Although most of the functions of aftercare are concerned with the improvement of mental health and the avoidance of relapses and rehospitalization (8), it can also serve the function of a stopover, as, for example, when the patient is waiting for admission to a longer term treatment facility. It may also benefit the patient who makes a poor adjustment on the inpatient unit and who does better in a less confined or less structured therapeutic milieu, such as is provided by partial hospitalization or by ambulatory treatment.

Aftercare has still another function; it invariably leads to a patient's family.

It has become a truism that it is not always the sickest member of the family who is hospitalized, and the aftercare patient may direct attention not only to the really sickest member of the family but, as a pathogenic influence, to the whole family. Indeed, an understanding of family interactions as well as the undertaking of family therapy may be important prophylactic factors in the sphere of mental health.

The orientation of the Department of Psychiatry toward normal and abnormal mental functioning has been based on dynamic psychoanalytic theory. Psychotherapy has been the mainstay of therapy although many other recognized therapeutic modalities have also been used. This is consistent with the point of view that under ideal circumstances one should strive to understand the dynamics, genetics, and the nature of the psychopathology and the clinical course of all emotional disorders. Psychotherapy is often a long and tedious process, which, in the inpatient setting, is incompatible with the brevity of the stay there. The mean hospital stay of inpatients has been constantly decreasing and lately has been as short as 25 days. If, consequently, psychotherapy is the treatment of choice, it has to be done in the Aftercare Clinic, although it is usually started on the inpatient unit. Our residents who are understandably interested in getting as much training in psychotherapy as possible, have been increasingly interested in their work in the Aftercare Clinic. Accordingly, they have been afforded the opportunity to carry some of their psychotherapeutic patients for as long as three years, although their formal stay in the Aftercare Clinic occurs during the first and second years of training.

In the course of time the distinctive function of the aftercare program has become increasingly evident. Linking both the inpatient and outpatient services, it is an integral part of a continuum and facilitates the transition from one to the other. This transition from hospital life to life in the community, for example, requires a major adjustment of which the staffs both of the inpatient unit and of the Aftercare Clinic must be aware (9). The patient usually needs help from both services to make the transition smooth and effective. No less difficult may be the converse, namely, the transition of a patient from the "outside world" to the hospital. The preparation of him and his family may take long and diplomatic persuasion before they are all convinced of the need of hospitalization. Even then, it is not an uncommon experience for a fearful patient to refuse admission at the last minute or to sign out shortly after his arrival in the inpatient unit.

Upon discharge from the hospital the patient is switched from maximum to minimum care, from complete protection to complete exposure, from relative isolation to full interaction, and from a therapeutic milieu to social and familial pressures which often have been pathogenic and contributory to his hospitalization to begin with. No wonder that the transition period is critical to the patient and that he may respond with a worsening of his condition and at times with psychiatric decompensation. Most rehospitalizations occur during this transition period in the first few weeks of aftercare. Consequently, nothing is more important during this period than a conscientious effort to effect a lessening of psychologic pressures, whether exogenous (familial and social) in origin or endogenous.

What is at times insufficiently appreciated is that similar pressures exist for the treating physician, usually a resident in training, who enjoyed close supervision while the patient was in the hospital and who is much more on his own when working in aftercare. From being able to see his patient as often as he wished, the doctor now sees him once or at most twice weekly. From having a different preceptor for each case for one hour weekly he now has to adapt himself to merely one preceptor for his whole caseload, sometimes voluminous, for one hour a week. Although consultation is always available, the resident in the Aftercare Clinic is being trained to be able to function on his own as much as possible under conditions that tend to approximate those in private practice. Emergency situations with newly discharged patients are a common occurrence and the budding psychiatrist may be in as much need of support and help as the newly discharged patient who is trying to make his way back to the community. The continuity of therapy and therapist help to overcome these crises to some degree. Later on, the aftercare phase of treatment may disclose other difficulties involving either the doctor or the patient or both (9). While the patient may have made a good adjustment in the "outside world" where he functions fairly well, and although he continues his psychotherapy, in the face of certain stresses he may encounter severe anxiety or other manifestation of mounting tension for which he seeks relief. At such moments he may be tempted to seek rehospitalization, while at the same time feeling that such a move would signify failure. On the other hand, the resident psychiatrist, anxious to achieve certain goals in order to prove to himself and to his preceptors that he is a good therapist, may react with hostility to his patient's new difficulties, viewing them too as a sign that he, the doctor, has failed. In such a climate an atmosphere pervaded by considerations of success and failure rather than of well being and suffering bodes ill for the entire therapeutic endeavor. The patient may react by dropping out of treatment and the resident by revealing his wish to get rid of the patient, for example, by suggesting rehospitalization in a different institution or by recommending discharge from the Clinic (9). Alert preceptorship may head off such a situation before it proceeds too far.

Another obstacle to the therapist's goal may arise from his failure to understand his patient's motivation in attending the clinic. Therapy may go on smoothly, the patient continues to attend his sessions, and the resident is pleased with what seems to be his cooperation. Closer inspection, however, should make it clear that this desire to please does not arise from an interest in psychotherapy per se but from a desire to be allowed to continue to come to the clinic indefinitely. Indeed, if permitted, some such individuals will keep coming to the clinic for the rest of their lives (10). In time their original resident therapist may have left long ago and they will have "gone through" many successors, revealing the fact that who the doctor is does not matter too much, for the actual symbiotic relationship of such patients is with the clinic and any doctor. It may indeed be characteristic of such people that although they are often unable to enter into a close interpersonal relationship they can relate to an institution—school, civil service, hospital—to which they attach feelings that have been called "institutional transference" (11, 12, 13, 14). Experience has shown that such individuals can weather many types of crises when assured of the knowledge that the hospital or clinic are available to them. And although technically they may have been discharged from the clinic, they have been assured that it is always available to them in time of need. As a consequence some return for brief periods of help, regain their equilibrium once more and are again discharged. In a way a "club" of former patients of the Aftercare Clinic is in existence based on the figurative ties of institutional transference. The preventive aspects of institutional transference are evident. What has been done was to establish the Aftercare Clinic as a base where the patient may feel at home and return to it at any time. This home base is the place where he receives the kind of care that suits him best. The internalization of the Aftercare Clinic by our patients as an institution alongside other institutions like the church, the school, the place of work, etc. will remain a mighty aspect of support until more creative and effective ways of handling mental illness are discovered (12, 13).

In contrast, there are a number of cases who, after careful screening, can be deemed suitable for more than merely supportive measures and for whom long term intensive psychotherapy is the method of choice. Our criteria for such decisions depend upon several considerations, one of which is whether we are "satisfied" with a patient's apparent recovery from the acute psychiatric condition for which he has been hospitalized, or whether, beyond that recovery, we seek to effect some change in his personality which hopefully would prevent future recurrences. Sometimes relatively modest changes may yield impressive returns in this respect, yet at other times, what look like major changes wrought by psychotherapy do not appear to ward off repetitive decompensations and attendant rehospitalizations. The latter is sometimes precipitated by environmental or situational factors, and if attention is not paid to these problems the possibility of recurrences and rehospitalization is greatly enhanced. In light of the fact that it is often not merely the individual who needs attention but the social setting, notably the family, the Aftercare Clinic has been engaged in providing family therapy and group therapy as well as individual psychotherapy.

Psychotherapy is not the only modality of aftercare, however. Drugs are widely relied upon and almost every patient who arrives from the inpatient unit is on medication. This in itself creates something of a problem because of the temptation to keep the patient on a drug as a "safety measure" rather than to ascertain from time to time whether he still requires it, and, if so, at what dosage. Drug management requires the watchful eye of each preceptor. It should be emphasized, moreover, that although the advent of psychopharmacology in the early 1950's made a great difference in many aspects of the psychiatric scene, it did not obviate a basic reliance on psychotherapy as a form of treatment, for, at best, drugs should be viewed as an adjuvant. The frequently quoted statement by Freud that pharmacotherapy will eventually be the answer to psychiatric therapy still has to be proven. In the meantime drugs have helped in some ways but have created problems of their own. In terms of aftercare, drugs are most helpful in maintaining the functioning of severely psychotic individuals outside the hospital. For these patients the psychotropic drugs are an undisguised blessing and their use has to be seen as a life-long measure on the same scale of significance as the use of insulin by the diabetic.

From the foregoing it should be evident that, as in all psychiatric practice, the goals of therapy in the Aftercare Clinic need to be delineated as rapidly as possible, and that they should be kept within the confines of what is feasible, as far as the latter can be determined (5). Such considerations will determine the nature of the therapy prescribed. Often changes in the psychopathological picture have to be given up because of the fixity of the illness, and improvement of function has to be aimed for (5). Long-term goals may have to be postponed or even abandoned and short-term temporary gains may have to be substituted. To summarize aftercare psychotherapy: It is tailored to fit each particular patient; it is always supportive, often brief, occasionally intensive, usually goal directed, and limited in scope. Negative transference is avoided, positive transference is allowed to stay on and is not tampered with; and when personal transference is not readily apparent, institutional transference is relied upon. Basic changes in the underlying personality structure are welcome if they take place but are not usually aimed for. Improvement in symptomatology and psychopathology are aimed for but not insisted upon if difficult to achieve. Improvement of functioning with a return to premorbid homeostasis are basic criteria for successful therapy (5, 8). It must be remembered that there are many mentally sick people in this world, some even afflicted with delusions and hallucinations, who nevertheless manage to function fairly well, derive some pleasure and satisfaction out of life, and may even be useful members of society.

The future of aftercare is inextricably linked to the future of psychiatry. It is becoming apparent that socioeconomic approaches, although indicated and necessary to combat poverty and elevate the nation's standard of living, are not capable of eradicating mental illness. Moreover, as useful as the mental health center may prove to be, mental hospitals will not cease to be needed. Hospitalization, although unavoidable at times, is still often as disruptive in terms of a person's place in the community and at home as it is curative in terms of psychopathology and restoration of function and skills. There is evidence that with proper attention and care most episodes of acute mental illness can be treated in the patient's home with good results and without disturbing the patient's social and familial homeostasis (15). The psychiatrist's function is not about to be restricted to that of a consultant only while therapy is delegated to the indigenous mental health worker. As useful as the concept of mental health may be in terms of prevention, it is not about to eradicate mental illness which requires all the skills of the well-trained psychiatrist as a therapist. Individual psychotherapy is not about to disappear in face of the flood of reports about the wonders of all sorts of group interventions. In all these currents and crosscurrents aftercare has an assured role to play, either as a short or a long therapeutic procedure. Psychiatric departments in general hospitals have been in the forefront of catering to the need of short hospitalizations in terms of diagnostic evaluation and reintegration of function, regardless of whether the mental illness has been an isolated episode or based on underlying chronicity. Neurotic chronicity does not necessarily require chronic aftercare as may often be the case of psychotic chronicity. The neurotic often functions well and can often lead a fairly normal and productive life. Aftercare with these patients should be of short duration. They should not be permitted to drop out because of the therapist's insistence that they need "more treatment" nor should they be permitted to cling to the clinic for the rest of their lives. Aftercare should be limited to the transitional period from hospital to community and the orientation of how best to use aftercare facilities in terms of future needs. Yet there is little doubt that psychiatry is moving away from its bed-oriented approach and its emphasis on inpatient services. Ambulatory psychiatry is increasingly becoming the method of choice, with the inpatient facility available as a "backup" when the need arises (16). Aftercare is more and more the outpatient custodian of all those who have had at one time or another the need to be hospitalized (5). Hopefully, it may continue this role and help to restore safely the greatest number of individuals to some degree of participation in the community.

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Trends in Suicide Research

PAUL FRIEDMAN, M.D., Ph.D.

> *And here, poor fool, with all my lore*
> *I stand no wiser than before.*
> Faust

In contributing an article to a volume honoring my old friend Dr. M. Ralph Kaufman, I cannot resist straying away from my assigned topic for a moment to reminisce briefly about an experience I shared with him in the fall of 1949. Together with Dr. Dale Cameron, then of the United States Public Health Service, we went to Israel on a psychiatric mission. The newly created Israeli government had requested a survey of the psychiatric needs of the country, faced as it was with large numbers of severely traumatized immigrants, children and adults, mainly survivors of the Nazi holocaust.

It was an unforgettable, challenging experience. What a contrast there was between the biblical serenity of the Judean hills and the harsh realities of the victimized children, estranged from their heritage, orphaned by the loss of their families, and in dire need of new attachments! This was indeed an all-consuming endeavor, working endless hours together with our Israeli confreres in a common search for solutions to problems which mankind should never have inflicted upon itself.

I would have liked to write about all this here, our psychiatric odyssey through the old settlements and new kibbutzim, from the old cradle of mysticism, Sefad, to the most modern dwellings just in the process of construction for the latest arrivals from the DP camps of Europe, Cyprus, and Morocco. In such critical situations, people get to know each other better than under normal conditions. And in this situation of total crisis, Dr. Kaufman showed not only great clinical acumen, but also unusual sensitivity and empathy for the plight of those whose survival was attained at a terrible psychological cost. However, I must forego further narration of those memorable events which eventually took the form of a joint report concerning the mental health conditions of the new State (1), and turn my attention to my present assignment, namely to the problem of Suicide Prevention.

My visit to Israel in 1949 was not my first encounter with Dr. Kaufman. Ten years earlier I had become acquainted with him when I joined the staff of the Committee for the Study of Suicide (2, 3), which had been organized by Dr. Gregory Zilboorg in 1935 with a grant from the late Marshall Field. Studies were conducted simultaneously in New York City (Bellevue and New York Hospitals); Denver (Psychopathic Hospital); Chicago (Institute for Psychoanalysis); and near Boston (the McLean Hospital, then in Waverly, Massachusetts). The projects to organize similar studies abroad (Vienna and Budapest) had to be abandoned because of the political cataclysms of the mid-thirties. Historical and anthropological investigations were to be supervised by Dr. Henry E. Sigerist of Johns Hopkins University and Dr. Edward Sapir of Yale.

A special aspect of the overall program was a study of the New York City Police Department undertaken at the request of Mayor La Guardia, because of the alarming rate of suicide among policemen at that time (4). Zilboorg's project was indeed a most impressive and courageous adventure in light of the ambivalence and outright antipathy to the theories and principles of psychoanalysis which still existed all over the world and especially in the United States. In fact, no sooner had the principles of this new organization been announced in a press release than some of the directors threatened to resign were the investigation to be based exclusively on psychoanalysis. Thus, the original program had to be amended and other methods of exploration supplemented. The original idea of awarding grants for ambulatory analytic work had to be confined to two institutions only—the Chicago Psychoanalytic Institute directed by Franz Alexander and the McLean Hospital in Boston where Dr. Kaufman conducted the psychoanalyses of suicide patients. The work of the Committee was terminated by the outbreak of World War II. With the exception of the Police Department study, the other records have not yet been published. The Zilboorg Archives, which represent an invaluable collection of clinical material, are in the custody of this writer. They have been recommended for microfilming by the National Advisory Mental Health Council, but unfortunately, the promised funds have not been forthcoming.* Years later, through personal contact, I discovered that Dr. Kaufman, like myself, shared the same admiration for the historical undertaking of Zilboorg. It should be observed, however, that the opposition to his project went beyond the matter of psychoanalytic methodology—it embraced the subject itself. Indeed, how unpopular research in suicide was at that time can perhaps best be seen in the fact that even Durkheim's (5) classic had not yet been translated into English and therefore the sociological theories of the problem still remained a terra incognita for the English speaking investigators. (It was not published in English until 1950.) And yet Durkheim's theories were the only ones that governed the sociological scene. In fact in 1934 when Zilboorg conceived his research project, there were only a few publications available on the subject of suicide in the medical psychiatric literature in the United States, namely, one by Jameison and J. H. Wall, "Some Psychiatric Aspects of Suicide" (6), and another by Menninger, "Psychoanalytic Aspects of Suicide" in the *International Journal of Psychoanalysis* in 1933 (7). Dublin and Bunzell's book, *To Be or Not To Be* appeared in 1933 (8). Zilboorg's paper "Differential Diagnostic Types of Suicide" was published in 1936 (9).

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* The microfilming of this material would have insured the permanence of this collection for pragmatic and reference purposes, especially for investigators interested in research of suicidogenic factors in depth. A follow-up of the patients who had undergone treatment in depth would have perhaps shed light on the role that the transference processes play in the therapy of the individuals with deep-seated aggressive propensities. Documents and transcripts executed with such a high degree of objectivity are rarely attainable in research on psychotherapeutic techniques, especially in the treatment of suicidal patients. Since this material was collected from a variety of hospitals in different areas in the United States, it represents a cross-section of the underlying problems involved (psychological, sociological, and ethnographic).

In a monograph (10) published in 1935, I attempted to show that the resistances the scientific world has manifested towards suicide throughout the ages have often changed in form only, but not in content. Indeed, it would seem that all scientific disciplines that concerned themselves with suicide were imbued with the old deterministic philosophy (of course not the biological one) which looked to supernatural forces in the outer world for explanations of human conduct, including the causes of suicide. Suicide was believed to have been caused by cosmic, climatic, and telluric influences (an opinion not infrequently heard today). The observation according to which the frequency of the suicide rate seemed to be greater in the spring than in the other seasons gave rise to the conclusion that there existed a simple causal relationship between the two.

Such ideas were rapidly accepted as plausible explanations for the suicide phenomenon. One need only recall Montesquieu's (11) famous theory expounded in "L'Esprit des Lois" (Laws against those who kill themselves) to become aware of the importance which that writer ascribed to cosmic factors. He naively believed that suicides in England are only due to the bad climate, an assumption which made it possible for him to speak of a "malady of climate."

There is no doubt that the Belgian astronomer and statistician, Lambert A. Quetelet (1796—1874) was influenced by Montesquieu in viewing the occurrence of suicide as an entirely constant phenomenon having no relation to the will of men, and hence arrived at the pessimistic conclusion that the number of suicides is a fixed and immutable tribute laid upon humanity: "It is a budget which is paid with frightening regularity" (12). This quotation, fraught with resignation, may be considered a classic and remarkably illustrative example of the deterministic point of view on the question of suicide. Quetelet's sophistry has finally proven to be paradoxical: The very same statistical figures to which he refers contradict the principal of constancy and the laws he claims to establish.

This is not an isolated example; we could cite many to demonstrate how erroneous all of these deterministic hypotheses were, all of which started from a false premise: They sought for causes in external influences and supernatural forces. The whole conceptualization was nothing more than a rationalized deep-rooted resistance to the problem, a means of avoiding the discovery of the real "determining tendencies," as it were.

Much as I would like to deal in fuller detail with a variety of hypotheses which have been offered to explain the suicide phenomenon, I must forego them in this limited space. Let us turn now to the studies and research which have been made in the field of medicine.

There was much activity in the early years of this century concerning the relationship of pathological anatomy to the problem of suicide. A very lively polemic took place when the concept of lymphatic constitution or status thymicolymphaticus was discovered by the pathologist Paltauf in 1900 (13). This was a morbid condition of the human organism characterized by hypertrophy of the lymphatic apparatus, a narrowing of the aorta, general adiposity, hypertrophy of the brain, and other organic abnormalities. Many anatomists and pathologists, attracted by this beguiling, if fanciful, "psychosomatic" conception, worked very hard verifying Paltauf's findings. The man who dominated the scene at that time was the Viennese pathologist, Bartel (14) who, after having performed numerous autopsies, found that those abnormalities were consistently present in the bodies of persons who had either committed suicide or otherwise died suddenly. When Bartel's theory was published in 1910, it sent a horde of researchers hurling themselves upon the corpses of suicides in order to look for the stigmata of self-destruction. A lively dispute ensued about the hegemony of the constitutional stigmata. The Russian scientists seem to have shown special affinity for the constitutional theories. It ought to be mentioned at this point that Russia was then experiencing a suicide epidemic, especially among youth, and their scientists were searching for clues. The famous Russian scientist, Krjukoff (15), came up finally with a theory which he claimed to have been an outgrowth of 25 years' experience. He not only was able to confirm Bartel's observations, but added some new ones, notably some additional abnormal stigmata to the already existing "suicide syndrome." Concurrent investigations in the field of craniometry revived the old hypotheses of phrenology which induced the Russian scientist to look for suicide stigmata in the configuration of the skull. "The primary cause of all the reasons leading to suicide," declared Krjukoff, "consists in some irregular activity of the brain; by trammeling the brain and impeding its normal development, the configuration of the skull is solely responsible for such functional irregularity; consequently, circulatory disorders are the fundamental factor." Krjukoff claimed that a premature sclerosis of the vessels was also found in the bodies of suicides. He drew a parallel between suicide and mental disease, stating that the same stigmata of cranial and cerebral degeneration are to be observed in both cases. The fact that the number of suicides did not correspond to the frequency of the cranial configuration which he described did not shake Krjukoff's hypotheses in the least. Firm in his convictions, he was able to circumvent this objection in advance by comparing suicide to tuberculosis and pointing out that the mortality figures for the latter also did not correspond to the frequency of the disease. He believed that, as with tuberculosis, there exist predispositions to psychosis in general and to suicide in particular, but that the percentage of their incidence is relatively small. In other words, an individual's constitution or a certain configuration of his cranium would predestine him to suicide.

Such were the opinions expressed from the viewpoint of pathological anatomy as to the organic constitutional role in suicide causation. With all apparent sincerity, Bartel asserted that he had laid down "the anatomo-pathological foundation" for a correct appreciation of suicide. And yet the entire sophistry was based on a cardinal error, namely, on the inference of an analogy between suicide and sudden death caused by organic factors.

Reviewing these historical facts one wonders, indeed, how these investigators in their quest for truth succeeded in completely overlooking one important factor, namely that the corpses they dissected once also harbored a "soul." The more one considers how stubbornly these scientists were looking for causes of suicide exclusively in the mechanistic or external world and completely sidestepping the psychological aspects, the more one must conclude that this scotomization was a result of deep-rooted and unconscious resistances, which in some instances, at least, one suspects may have resided in a need for the investigator to deny his own occasional suicidal fantasies.

Undeniably there were around the same period a good many works which reflected a different attitude. Names like Heller (16), Sihl (17), Kollarits (18), and a few others ascribed to the organic stigmata only a secondary role in causation. They all came to different conclusions after performing hundreds of autopsies on suicides. They began to differentiate between the real causes and the purported, immediate reasons which had prompted the act. Kollarits even regarded the immediate reason as an external circumstance to which but little importance should be attached. In his estimation, it was always the victim's "character structure" which alone determined whether or not one resorted to this last desperate action. And finally Placzek (19) advocated that research in suicide should proceed through a thorough and complete study of each individual case and not by a mere accumulation and recording of conjectural motives about the causes.

And yet the password "constitution" long remained a guise and convenient cover-up for the deep resistances which greatly handicap our thinking about suicide and its pathogenesis. Nineteenth century psychiatry had added more immutable stigmata to the "suicide syndrome." The belief that the problem of suicide could be solved by diagnosing it as some form of madness persisted. Bourdin (20), Esquirol (21), Brierre de Boismont (22), and even Krafft-Ebing (23) and Gaupp (24) all declared suicide a pathological act. Brierre de Boismont, who may be referred to as the father of the psychological autopsy so popular today, deemed it possible that there might be some suicides by those of sound mind whose "moral being" alone was impaired. The moral connotation, incidentally, has played a special role in suicide investigation, especially among the nineteenth century Italian criminologists and anthropologists.

The most profound study was made by Esquirol in 1827. While he, too, regarded suicide as an act committed in a state of delirium, his manner of viewing the problem was more original. He was the first to emphasize the psychogenic character of suicide. He was also the first to stress the social and environmental conditions enhancing and precipitating suicidal impulses and dispositions. Difficulties in the social sphere are designed to upset an individual's emotional and "moral" equilibrium and provoke psychic disorders. Esquirol's views as to the reactive and psychogenic character of suicide did not prevail for long. His theories underwent radical change under the influence of new trends in psychiatry which on the one hand placed greater emphasis on the organotoxic etiology of psychological disturbances, and on the other hand ascribed even greater importance to hereditary and constitutional factors.

How much these concepts have come to predominate research in suicide could be seen in the "Psychologie Pathologique du Suicide" by Achille-Delmas (25).

In this elaborate work, published in 1932, Delmas set himself the task of proving that sociological methods are without foundation, and contested, especially, Durkheim's findings and the final research by Halbwachs. His conception can be summarized by stating that suicide was exclusively determined by physiological factors; he even believed that the origin of anxiety is to be found in the "internal physiological motivation." Looking back from our contemporary vantage point, one is struck by the complete lack of a collaborative effort and attitude among the various investigators of suicide during that era.

As I pointed out elsewhere, Durkheim's criticism of the major psychiatric theories then available to him was entirely justified. Those purely descriptive and static explanations were not persuasive enough to explain the phenomenon of suicide. One is entitled to speculate that Durkheim might have taken a different position with regard to psychological explanations had he been familiar with the relevant contributions of modern dynamic psychology and of psychoanalysis. But unfortunately when Durkheim's classic "Le Suicide" was published in 1897, psychoanalysis was still in its early stages of development and little, if any, of the psychoanalytic literature available dealt explicitly with this problem.

It was not until 1910 that psychoanalysis began publicly to debate about suicide. The Symposium (26) sponsored by the Vienna Psychoanalytic Society on the 20th and the 27th of April of that year proved to be a milestone in the development of our thinking on suicide. In addition to Freud, the participants included Alfred Adler (27), Wilhelm Stekel (28), J. Sadger (29), Josef Friedjung (30), Ernst Oppenheim (31), and others.

In this historical sketch, it is most relevant to say a few words about the events that led to the Symposium. At that time, Europe allegedly witnessed an upsurge, to which Vienna was no exception, of suicide among young people, especially high school and university students. The schools and universities became the targets for public attack and the educators were made scapegoats for the suicidal propensities of young people. Aroused by these accusations, the educators began a vigorous battle to refute the charges leveled against them and to defend the dignity of the schools. The pedagogues turned to the behavioral sciences for rescue. And so it came to pass that a teacher of classics, Professor Ernst Oppenheim, initiated and organized this Symposium, thus challenging the medical world to focus on suicide. It is not possible to review the entire proceedings here so I must refer the reader to the recent translation of the original text (32). For our purposes, I must limit myself to highlighting a few important moments of the meeting.

Oppenheim's most significant contribution was to suggest that family life, the family constellation, is a decisive factor in the etiology of suicide among young people. He vehemently refuted all accusations and charges leveled against teachers, maintaining that it was a deliberate shifting of public attention from the fact that suicidal acts committed by people between the ages of 15 and 20 are eight times more frequent than among the general population. He was most emphatic that the terms "student suicide" and "secondary school suicide" erroneously implied that the motive for every student's suicide lay in the student's relationship to the school. "Youthful suicide is not a local phenomenon, and is not as recent as newspaper writers imagine. It first emerged during the Renaissance. If we were to assume that harsh discipline in schools is as antagonistic to the life impulses as many critics assert, how can we explain the fact that suicide among the young is increasing, even though school discipline has become milder?"

Of the many facets of the problem of suicide which were discussed at the Symposium I wish to mention only two of the more significant ones. The first was the concept that sexuality might play a role in the developmental ideation of suicide. Surely it was without precedent that psychosexual crises and heterosexual or homosexual conflicts should be regarded as causative factors in the suicide of youth. (Of course, we must be aware that at that time the "libido theory" was still grounded in chemico-mechanistic conceptions and that "ungratified libido" was believed to be directly transformed into anxiety in the young person and was thus responsible for the suicidal act.) The second was the momentous and bold suggestion of Stekel concerning the role of the so-called "talion principle" (an eye for an eye, etc.) in the genesis of suicide. He was the first to hypothesize a relationship between homicide and suicide when he asserted that "nobody kills himself who did not want to kill another or at least wished death to another." The full significance of this idea, now so universally accepted and so basic to our understanding of the interplay between murderous impulses and suicidal drives, could not be completely grasped until 1917 when Freud formulated his theory of sadism in "Mourning and Melancholia" (33).

In this seminal contribution to our understanding of depression, Freud explained that pathologic depression takes place when the subject identifies himself with an internalized object that is both loved and hated; and that the self-accusation and self-deprecation so characteristic of depressed persons are in fact directed against this introjected object. He came to the conclusion that "it is this sadism, and only this, that solves the riddle of the tendency to suicide which makes melancholia so interesting—and so dangerous. It is true we have long known that no neurotic harbors thoughts of suicide which are not murderous impulses against others redirected upon himself, but we have never been able to explain what interplay of forces could carry such a purpose through to execution."

By virtue of this clarification of Stekel's statement, Freud was able to shed decisive light on the observations and statistical findings of the nineteenth century sociologists (Morselli (34), Ferri (35), and others). The conclusions, for example, that the "antagonism" or inverse relationship between suicide and homicide was only an apparent one and that both arose from the same source, from the same causality, no doubt astonished contemporary investigators. A dynamic explanation was now provided by psychoanalytic theory. While all of Freud's ideas have served as prototypes for the many investigators who followed him and have been clinically verified again and again by the lasting contributions of such authors as Abraham (36), Federn (37), Brill (38), Nunberg (39), Bernfeld (40), Fenichel (41), and many others, the scope of the original formulation has since been broadened. Thus while often enough suicide represents a displacement of aggression against the self, "murder in the 180th degree", psychoanalysis has also recognized that the suicidal act has usually more than one meaning and that the element of aggression may play a greater role in some cases than in others. There is indeed a wide range of nuances and degrees with regard to the sadistic quality of the suicidal act, which may be reflected by the specific method used in self-destruction; the individual does not merely want to kill himself, he wants to kill himself in a specific manner by a special method (drowning, poisoning, shooting, etc.) The choice of the method represents moreover an area in which imitation plays a special role as can be observed in suicide epidemics. Cases have been reported, moreover, where persons who were thwarted in their suicidal attempts then abandoned them.

That suicide can be traced back to processes of identification with the loss of a love object at pivotal ages, such as at the height of the oedipal phase and at the beginning of puberty, was demonstrated by Zilboorg in his clinical observations, especially of children (42). The rationale of such an identification is the desire to be reunited with the love object. Incidentally, where the loss of the loved one has been brought about by suicide there is often an imitation of the method in the subsequent suicide of the survivor.

It was for the purpose of verifying and testing the validity of these psychoanalytic theories that Zilboorg organized the committee for the study of suicide in 1935. In the intervening years very little clinical research in depth has been undertaken to enrich our knowledge as to the basic dynamics underlying suicide and to enhance the therapeutic methods of our efforts to establish an effective prophylaxis.

Although numerous papers have been written and many projects organized throughout the United States and abroad in recent years, none has gone beyond repetitive statistical data and semantic speculations. Psychological research in depth came to a standstill a quarter of a century ago and clinical contributions based on psychoanalytic theories have become very rare. There is, for instance, much confusion in the literature and much sophisticated rationalizing around the definition and the concept of suicide itself, but our clinical and pragmatic understanding have not been enhanced. Many of these philosophical and dialectical discussions are interesting only as semantic exercise. To my mind, such efforts to delineate the issue of lethality and to postulate criteria differentiating between genuine and pseudosuicidal gestures are often misleading and fallacious. Paradoxically, such overextended excursions militate against the pragmatic goals of prevention. The patient who only yesterday in a fit of paroxysmal anger swallowed a few aspirins threatening to commit suicide, may tomorrow leap from the rooftop. The aspirin should not be regarded as a merely momentary and defiant gesture but an announcement of the emotional tornado gaining momentum within.

This brings us to the problem of suicide detection in general and, with it, the doctor's role in prevention. According to available estimates, approximately 75 percent of persons who commit suicide consult a physician within six months prior to their self-imposed death. This has been used as a basis for the argument that the general practitioner, if properly informed of the signs and symptoms of suicide, could play an important role in detecting potential cases. While it may be true that the doctor still resists confrontation with the problem, it is perhaps overoptimistic to expect him to be prophetic. Detection of suicidal trends is an extremely difficult process, and even experienced psychiatrists, familiar with a patient's life history and psychodynamics, are not always able to estimate correctly the extent of risk. Nevertheless, the medical doctor could play a greater role in suicide prevention not only through the detection of danger signals but also through the provision of psychiatric first aid in emergency situations. While there are no absolute predictors of suicide, there are premonitory and prodromal clues by which the doctor can be guided. These may be divided into two major categories, the direct and the indirect.

Direct cases may be either verbal or behavioral. A threat of suicide or an overtly expressed preoccupation should always be taken as an indication of suicidal risk. The notion that an individual who talks about suicide never commits it is a misconception which is in diametric opposition to clinical experience. The fact that it persists despite its tragic untruth is based upon the motivation that lies behind it, namely, the desire to avoid anxiety. A verbal threat of suicide should be given special weight if a specific and notably lethal plan is mentioned.

Similarly a history of past suicidal attempts should be viewed as increasing the likelihood of a future attempt. Moreover, although many suicidal patients have a history of surviving a series of attempts, some of them apparently half-hearted, there is always the possibility that in such cases a subsequent, more determined attempt will lead to death.

The claim that to inquire about suicidal intention may trigger suicidal action is invalid, and unsupported, and, like other superstitions regarding suicide, reflect our own anxieties. It is particularly imperative for the general practitioner to be on the alert for the type of patient for whom he prescribes various antidepressant drugs and barbiturates. In this connection, mention should be made of the so-called suicide "cache" which is the accumulation of a lethal dose of drugs and/or articles, e.g., razor blades, knife, gun, etc., which could be used to commit suicide and are often hidden from the family and seldom divulged to the doctor. The patient may treasure a secret hoard of drugs as a "way out" should he feel his tolerance to adjust to life has been exceeded. The cache may never be used but its mere acquisition may militate against any genuine effort to resolve conflicts and adapt to reality.

With these objectives in mind, we organized our Suicide Prevention Center in September 1968.* It is our firm belief that more research and more appropriate methods are needed to penetrate the pathogenesis of suicide. More reliable diagnostic criteria and more pinpointed clinical detectors are imperative.

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* Dr. Stanley Friedman, Assistant Professor, Mount Sinai School of Medicine, and a member of the New York Psychoanalytic Society, joined me in this project in January, 1969. Grants were received from the following generous benefactors: Mr. and Mrs. Emery Klineman, Charles Simon Foundation, Mr. Sidney Elliott Cohn, Mr. and Mrs. Bernard Needle, and Peter Cats Foundation.

Any comprehensive program of suicide prevention must of necessity consist of two phases of operation: one, of research based on direct clinical observation, both phenomenological and dynamic; the other, of theoretical education for the resident in psychiatry, the student of medicine, and the general practitioner.

Our original aim was as follows: to study 200 patients admitted to the Psychiatric Service for an attempted suicide. Approximately 50 of these admissions were to be studied intensively by the project psychiatrists. This qualitative study in depth was to be a part of a larger series of researches including an evaluation of taped psychoanalytic sessions collected over the years by the Committee for the Study of Suicide.

Every suicide patient is immediately interviewed on admission with the help of a specially compiled questionnaire designed to obtain the life history of the patient in the context of his suicidal propensities. The questionnaire is particularly geared toward ascertaining developmental characteristics within the orbit of the family constellation. Suicidal propensities, homicidal impulses, violent behavior, and addictive patterns, as well as other acting-out manifestations can be readily detected. In interviewing a suicidal patient the time element is usually of great essence, for the patient is often in a state closely resembling a dream. Since the patient may rapidly lapse into a state of amnesia regarding his suicidal act, the precipitating factors should be retrieved as soon as the patient emerges from the suicidal aura. Delay in their elicitation may sometimes result in an irreversible loss of the opportunity to unearth material belonging to the very depths of the human psyche.

In compiling our questionnaire, we wanted to obtain orientation along the following lines:

1) The role of religious and cultural factors influencing or counteracting suicidal intent.
2) The role of current frustrations, disappointments, and feelings of guilt as causal factors (and the relationship of these to earlier predisposing factors.)
3) The role of psychosexual development (deviations), of alcohol, and of other addictions as influences upon suicidal impulses.
4) The effect of sadomasochistic behavior patterns, violence, and suicidal acts in the family history as predispositional factors.
5) The role of imitation and identification in suicidal ideation.
6) The role of revenge motives in the suicidal act, especially in the young.
7) The relation of the suicidal act to previous patterns of aggression against the self or against others.
8) Fantasy content related to the choice of method.
9) The psychodynamic role of physical injuries sustained in suicidal acts and their relationship to the masochistic Anlage of the individual.
10) Suicidal pacts and their mutual sadomasochistic interplay. (In this connection, it is anticipated that a study of the surviving partner of such a pact is likely to reveal homicidal impulses.)

The paramount goal of our research is to evaluate the effectiveness of various psychotherapeutic techniques—both short and long range—and, in this connection, to study the role of the transference in the treatment of suicidal patients. This research will include the appraisal of the existing psychometric tests and their usefulness in finding early criteria of suicidal propensities and potentials.

As far as the educational aspect of the project is concerned, we envisage theoretical lectures and seminars for the resident in psychiatry, the third- and fourth-year medical student, and orientation courses for the nonpsychiatric physician.

The resident will be exposed simultaneously to the theoretical framework and to direct encounter with the suicidal patient from the first year of training. He must be taught from the beginning that suicide is not an immutable, "hereditary" state of mind, doomed to end in disaster, but that it is an illness, a syndrome or a symptom like any other psychopathological entity—that it can be altered, influenced, managed and cured. It is further important that the psychiatrist be conditioned early in his professional role to master his own anxiety when treating a suicidal patient. Four years of training under sensitive and comprehensive guidance will help to equip the young psychiatrist with the understanding and empathy so essential to the care of the would-be suicide. Let us not forget that the ego of the suicidal patient is diminished and regressed. He is often too immobilized to reach out for help. He must be made to understand his underlying conflicts and the reasons for his renunciation of the self-preservation instinct. Without insight there can be no effective remission.

Among all the modalities available in modern psychiatry for the treatment of the suicidal patient, psychotherapy in depth remains the most effective method, especially in the treatment of the young. Chemo- and electro-convulsive therapies alone do not seem to reduce the incidence of suicide. It is a matter of fact that recent statistical data show that patients who have attempted suicide repeated their attempts more frequently after discharge from hospitals where they were treated by shock or pharmacological means alone than did patients who had the benefit of psychotherapy while hospitalized. This does not come as a surprise because, for the former patients, psychological insight was neither the goal nor the result of their therapy; their internal tensions and unconscious conflicts remained unexplored and were left in the same state of obscurity.

The lectures and seminars for medical students and general practitioners are intended not only to acquaint them with general theories of suicide and the management and psychotherapeutic goals, but equally to enlighten them by helping to overcome their own fears and resistance whenever confronted with the suicidal patient. Suicide is still shrouded in mystery and there is a remnant of superstition in all of us as to its nature. We still look for the supernatural, for fatalistic and immutable causes, apparently trying to deny that an individual may elect death by his own hand. This mechanism of denial provides comfort for the family and protects them against social and religious stigma. Contemporary culture continues to stigmatize the suicide as it did in the Dark Ages. Suicide should not be regarded as a moral issue but a medical problem.

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3. The author of this article joined the staff of The Committee for the Study of Suicide in 1939. The original membership of the Committee was as follows: Dr. Franklin G. Ebaugh, Professor of Psychiatry, University of Colorado; Mr. Marshall Field; Dr. Raymond Gosselin, Psychiatrist; Dr. Gerald R. Jameison, Medical Director of the Payne-Whitney Psychiatric Clinic of the New York Hospital; Dr. Karl Menninger, Director of the Topeka Psychiatric Hospital, Kansas; Dr. Herman Nunberg, Psychiatrist; Dr. Winfred Overholser, Director of the St. Elizabeth Hospital, Washington; Dr. Mortimer Williams Raynor, Medical Director of Bloomingdale Hospital; Dr. Henry A. Riley, Professor of Neurology, College of Physicians and Surgeons; Dr. Edward Sapir, Professor of Anthropology, Yale University, New Haven, Connecticut; Dr. Dudley B. Shoenfeld, Psychiatrist; Dr. Henry E. Sigerist, Professor of the History of Medicine of the Johns Hopkins University, Baltimore, Maryland; Dr. Bettina Warburg, Psychiatrist and Psychoanalyst; Dr. Gregory Zilboorg, Psychiatrist, Former Secretary of the Psychoanalytic Institute, New York City; Mr. Louis Weiss.
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Community Psychiatry at The Mount Sinai Hospital

MILTON R. SAPIRSTEIN, M.D., AND MORRIS H. BERNSTEIN, M.D.

Under the leadership of Dr. M. Ralph Kaufman, The Mount Sinai Hospital has made many imaginative attempts to serve the psychiatric needs of the surrounding community. In 1953, long before the word was in common usage, the principle of community psychiatry was initiated by Dr. Kaufman's proposal to undertake the psychiatric treatment of all the tenants of Carver House, a neighborhood housing project. The plan embraced the inclusion of clinic facilities within the housing then under construction. It was an idea born before its time; because of lack of interest, of money, and the opposition of many groups, this imaginative concept was abandoned and a great opportunity was lost.

In 1958, another attempt was made to offer psychiatric services to the community. At that time, a Division of Organization Psychiatry was established, with the specific purpose of training psychiatrists and related personnel in the mental health field to deal with the psychiatric needs of large community groups.

Because of its large staff and broad range of treatment opportunities it was felt that The Mount Sinai Hospital was in a unique position to provide psychiatric services and possibilities for research in a varied assortment of settings. Initially limited to organizations such as industries, labor unions, tenants' groups, financial groups, or religious orders, the program was called the Division of Organization Psychiatry. As such it carried out the following programs:

1. A study of the emotional aspects of the retirement program of a well-known liquor-producing company.
2. An analysis for the Port Authority of New York of the problems of evaluating candidates for the position of policeman with particular emphasis, with the aid of Rorschach studies, upon impulsive and antisocial aggressive behavior among these individuals.
3. A study of accident-proneness among personnel of a large department store.
4. An inquiry into absenteeism in an enterprise employing convalescent patients.
5. An actuarial study to evaluate the possibility of including psychiatric care in the medical program of the Health Insurance Plan of Greater New York (HIP).
6. A two-year study designed to investigate a seemingly excessive turnover of personnel in a New York advertising agency.
7. An attempt to evaluate the breakdown of scientists in industry. (This study was reported in the *Journal of the Hillside Hospital.*)
8. A study of the feasibility of providing psychiatric consultation and treatment for the 200,000 members of a labor union.

9. An analysis of the interpersonal reactions of the executives of several corporations.

In recognition of the fact that the expanding scope of community needs was an appropriate concern of a psychiatric department of a general hospital and as our experience developed and our program expanded, in 1965 the Division of Organization Psychiatry changed its name to the Division of Community Services. This expanded program was an especially meaningful undertaking for the Department of Psychiatry of The Mount Sinai Hospital for the following reasons:

1. The broad experience gained in the psychiatry of groups provided a wide range of experience in dealing with outside organizations which would become an invaluable asset in community work.
2. Our geographical position placed us in close contact with the problems of poverty, segregation, drug addiction and specialized problems of minority education. We did not have to seek out these problems; they would constantly come to our attention.
3. The unique position of The Mount Sinai Hospital with its large staff of psychiatrists, psychologists, and social workers made it possible to undertake very large projects without sacrificing professional status. (Many community service projects falter because of a lack of professional staff which leads to recurring makeshift staffing problems and constant improvisations.)

In keeping with this broader conception of the function of our Division were the following projects:

1. *Cooper Union Study.* This is a part of an ongoing study of the problems of scientists in industry done in conjunction with the Cooper Union School of Engineering. The main goal is to determine the relationships between (a) variables measured at graduation and (b) the success and creativity of the subjects during the first eight years of their careers. The variables measured fall into two major categories: cognitive and intellectual factors on the one hand and personality goals and values on the other.

In conjunction with this general study, data were collected including individual case histories of scientists who had received treatment in various facilities.

2. *Free Synagogue Counseling Service.* Originally designed as a marriage counseling service to the Free Synagogue, this project became a community service program. All cases which come within the orbit of Rabbi E. Klein and his staff and which require psychiatric services were seen at the Synagogue, treated if possible on a brief therapy basis, or referred to the proper agency.

3. *Sidney Hillman Health Center* (Amalgamated Clothing Workers Union). Working in close conjunction with the Mental Health Program at this Center our Division provided a psychiatric consultant who participated in planning and treatment. General hospital psychiatric facilities were also provided for this major union health center. In addition to rehabilitating their own workers, an opportunity for training in this industry was offered to Mount Sinai Hospital psychiatric patients. The project was later expanded to a Mental Health Rehabilitation Program in cooperation with the Central Labor Council (AFL-

CIO). This program led to a special labor award to the hospital for public service.

4. *Legal Aid Society.* With the encouragement of the Hon. Abraham Geller, we assumed a working relationship with the Legal Aid Society which provided free psychiatric consultation including courtroom testimony for indigent clients.

5. *Consultation with New York City Department of Welfare.* Growing out of a special consultative service for the Yorkville area of the Department of Welfare, Mount Sinai has been deeply involved in helping the departmental investigators who cannot cope with the many psychiatric problems of indigent relief recipients. As an outgrowth of his work on the project, Dr. Herman Tanner assumed the post of Chief of Psychiatry for the Department of Welfare.

6. *Consultation with 92nd Street YMHA-YWHA.* Under the sponsorship of the Division of Community Services, a medical-psychiatric consultative and treatment service is now being provided for the local "Y." This is offered to the residents of the Residential Center, as well as to the regular members of the huge transient group which utilizes the many facilities.

7. *Services to City University.* Psychiatric consultations are now being offered to the students of Hunter College. Drug addiction consultation and treatment for the Search for Education, Elevation, and Knowledge (SEEK) program of City University are also being offered by the hospital.

From the foregoing it is evident that for some time a viable Division of Community Services has been developing at The Mount Sinai Hospital. It has served as a valuable workshop from which psychiatric personnel receive training and practical experience in broad areas concerned with mental health problems and from which the community receives a wide range of services. Gradually the community has responded, as evidenced by the new projects that are being developed by the Division. Of these not the least in importance has been our contribution to the field of community medicine. Throughout our early experience it was abundantly clear that the Division would not flourish without community medicine; in recent years, under the leadership of Dr. George James, President, Mount Sinai Medical Center, Dean, Mount Sinai School of Medicine, and Dr. Kurt Deuschle, Chairman and Director, Department of Community Medicine, Mount Sinai Medical Center, the phenomenal growth of the Department of Community Medicine has given us an unusual opportunity to work with our medical colleagues. Our division now participates in all the new projects which Community Medicine undertakes. Our goal has been to introduce the concepts of mental health to other health services in the community. Two such examples presented here to demonstrate the role of community psychiatry are the Health Care Unit (originally called Family Practice Unit), which followed in the tradition of the Liaison Service, and the previously mentioned Carver House Project designed to bring psychiatry into a mutual and coordinated effort with other departments of the hospital.

Originally established in 1967 by the new Department of Community Medicine, the Health Care Unit was planned as the clinical division of that department. Its goal was to provide effective and efficient delivery of comprehensive health services to a specific segment of the population, and from the beginning, mental health services were included as an integral part of the program. Thus, the wholeness of the individual was recognized both in principle and in practice. Disturbances in life situation, whether resulting from intrapsychic disorder or from environmental influences, were considered neither before nor after physical disturbances of health, but simultaneously. This recognition of individual wholeness required a staffing pattern in which the psychiatrist became an integral part of the health team. He was not a consultant who came in from somewhere else—he was "inside" from the beginning. A similar integral role was played by other physicians on the team—internists and pediatricians—and by social workers, nurses, and indigenous "health advocates" (nonprofessionals who live within the patients' own community and who are chosen for their aptitudes and interests). A supporting staff performed administrative and clerical functions. As the staff worked together and came to know each other, a strong group identification developed with resulting team spirit and a strong motivation to carry out the objectives of the unit. Staff members came to recognize an inner core or cadre of the team, and an outer group whose participation was seemingly of less importance. The considerable turnover of the latter met with little reaction from the remaining group, but the departure of any member of the "core group" was regularly followed by manifestations of depression. Staff conferences were devoted to case material, and also to a beginning discussion of staff–group interaction. This was a natural step in the group's development since it followed a disucssion of the patients' interaction in their own family group. The psychiatrist contributed to the understanding of the dynamics of the patients' interaction as well as the staff's.

Officially, patients of the unit were seen by appointment, and with a minimum of waiting time. However, as time passed there was an increasing number of drop-in visits without appointments. This was possible because the unit was open and staff was present from 9:00 A.M. to 5:00 P.M., and because patients typically developed a feeling of relatedness to more than one staff member. We learned that for many of our patients, visits by prearranged appointments were almost impossible. This required of them a degree of organization and discipline not demonstrable in any area of their lives. A visit to the unit occurred typically when the subject felt unable to cope with pain, anxiety, or depression, or with a life situation seen as threatening or overwhelming. Even psychiatric drop-ins were easily dealt with. Those who wanted to see the psychiatrist personally learned exactly when he was available. Others were seen by members of the staff who had the opportunity to discuss the patient and his family with the psychiatrist at frequent intervals. In general, no sharp distinctions were made between "psychiatric" and "nonpsychiatric" patients, although certain subjects were identified as having key problems in the psychiatric area, and therefore as primarily the psychiatrist's responsibility.

When the program began there was only a vague idea of what psychiatric problems would be presented and of how they would be handled. During the two-year period of this program's existence the psychiatrist had direct interviews with approximately 100 patients, and participated in staff discussions of many more. The maximum case load of the program was 300 families. Initially, patients were referred to the psychiatrist by other staff members because of physical complaints for which no physical basis could be found. In time as the staff was alerted to watch for positive evidence of emotional disturbance related to marriage, children, jobs, etc., more patients were referred for these definitive problems.

Patients referred to the psychiatrist were interviewed for evaluation one or more times. Since about two-thirds of the patients were of Puerto Rican origin, there was often a language barrier. Occasionally an interpreter was used, especially for initial interviews, but it was found that many patients who claimed to speak only Spanish were able to communicate well in English after the interviewer tried to conduct the session in Spanish. Many effective interviews were in "Spanglish," and the psychiatrist made the interesting observation that sometimes the mutual groping for a common language helped in developing a positive relationship.

Most patients were seen from one to five times; more often than not at least one additional family member was also seen. After evaluating key factors in the situation, an attempt was made to intervene in such a way that the patient could then cope with the current crisis. This might involve environmental manipulation and/or a variety of psychotherapeutic techniques such as reassurance, counseling, role playing (as a powerful authority figure on whom the patient could depend in time of crisis, the psychiatrist could be very effective), and offering simple interpretations (e.g., making patients aware of suppressed rage or guilt). Medications were expected by patients and were freely used, the choice often being influenced by their attitudes (often culturally determined) toward various medications. Thus, in addition to the usual armamentarium of tranquilizers and antidepressants, there were also placebo injections, and even prescriptions for proprietary tonics widely publicized in the mass media.

Patients were discussed with other staff members, both in formal conferences, and informally in the clinic area. Much of the treatment was delegated to other staff members without regard to their professional backgrounds. In fact, the nonprofessional "health advocate" was used increasingly. This delegation of the psychiatrist's role was made possible because patients usually developed a positive relationship with several members of the unit staff rather than to one individual, or to the entire hospital for that matter. Indeed many patients revealed strong negative feelings toward the hospital but nevertheless saw the unit staff as "good." It would appear that this positive relationship, which is so important therapeutically, develops most readily when staff morale is highest, and high staff morale, in turn, is fed by the patients' positive relationship and responsiveness to staff.

Unfortunately, it was necessary to close the Health Care Unit in 1969 for lack of funding, but most of its staff still work in the hospital, and its orientation and approach continues in their current work.

A brief case history from the Health Care Unit will illustrate some of the foregoing ideas:

José S., age one, was referred to the Health Care Unit pediatrician because of recurrent upper respiratory infections with otitis media. José had been born at Mount Sinai, and his mother's chart indicated that she had had a severe postpartum reaction with expectations of impending death, severe anxiety, and visual hallucinations concerning her own dead father who was beckoning her to come and join him. José's mother, age 27, had been depressed and fearful as long as she could remember. She had had very little social life, and when her husband asked her to marry him, she accepted with amazement and gratitude, although he was only 18 (four years her junior) and had no job at the time. The husband, now 23, worked regularly as a grocery clerk and seemed devoted to his family, which also included a 4-year-old daughter. After work each day, he returned home, played with the children, did some house work and cooking while Mrs. S. sat and complained about her unhappiness. They never went out together and she usually resisted his sexual advances. She complained about her contraceptive pills which she felt were depressing her. The family was referred to the psychiatrist as soon as her history of postpartum psychosis was known. The psychiatrist chose the contraceptive problem as the most accessible key issue for this family. After discussion of the available techniques, and Mrs. S.' apparent acceptance of all of them, she was referred to the gynecological consultant. He, however, found her unwilling to accept any contraceptive method. Mrs. S. then told the psychiatrist she could not trust any method, and was sure she could become pregnant with any of them. Her fear was then seen as one of being overwhelmed by the experience of pregnancy, delivery, responsibility for child care, etc. In addition she appeared to harbor unresolved resentment and guilt in relation to her dead father.

This woman was seen about 25 times by the psychiatrist over 18 months. During this period the entire unit staff also worked directly with her. We made it possible for her to withdraw and regress when her symptoms showed that this was necessary. We explained her needs to her and to her husband, who was becoming impatient with her. We provided homemaker services, and she had two periods of hospitalization on the Psychiatry Service. We emphasized that these measures were temporary, and that independent functioning was always our goal. We saw the S. family as a hardcore, multiple-problem family in which the most significant factor was Mrs. S.' inability to function in her assigned roles due to her psychopathology. When this improved as a result of a considerable input of coordinated effort by the unit staff, the entire family situation improved. Thereafter they needed only minimal help in order to maintain the improved functioning.

A second program which illustrates the role of Community Psychiatry at Mount Sinai is the Methadone Maintenance Treatment Program for heroin addicts. Heroin addiction is recognized by professional health workers, and by the lay population of East Harlem which surrounds Mount Sinai, as the most serious of all health problems in the area. In 1969 Mount Sinai responded to this challenge by starting a treatment program to be limited to 50 addicts. This was soon increased up to 100 patients and is now to be further increased to 500. The Department of Medicine was administratively in charge, and the program was located in two small unprepossessing rooms in one of the hospital's oldest buildings.

A staff was recruited consisting of a part-time internist as director, a third-year medical resident who shared the medical duties, a part-time psychiatrist with an interest in Community Psychiatry, a head nurse with assistance from a per diem nurse and occasional student nurses, a research assistant (in methadone program language this is the term for a former addict under treatment in another methadone program), and a secretary-clerk (a young woman who took time off from her work toward a Ph.D. in the history of ideas). From time to time medical students and two psychiatry residents also worked in the Program.

The shortage of methadone treatment facilities in New York city was immediately demonstrated. Within two weeks after the program started, and without any publicity, there were over 160 applicants. Our criteria for acceptance of a patient were based partly on already existing successful programs: a minimum of three years of continuous addiction to heroin; at least 20-years-old; no mixed addictions; living in East Harlem, preferably with own family; employed or housewife; not dropped from other methadone programs.

Originally, psychiatric screening interviews were done on all patients who met the above criteria and who had passed physical and routine laboratory examinations. This was abandoned since applicants are not excluded for psychiatric reasons except for such gross disturbances as hallucinations or suicidal behavior, which can be recognized in most instances by the nonpsychiatric staff. Furthermore, it has not been possible to use the screening interview as a predictor of future disturbed behavior, or of success or failure in the program. This coincides with the experience of psychiatrists in other methadone programs.

Indeed interviews with addicts are full of pitfalls for the unsuspecting psychiatrist. He is likely to be told a logical and well-organized account of the addict's life and activities, only to learn much later that most or all of the story was fictional. This is often true even when there is no obvious advantage to the addict in telling the fictional story over the true one. This can be understood when it is remembered that most of the addict's life is necessarily spent in illegal activity: obtaining illegal drugs, selling or distributing them, getting money to pay for them. For any of these he can be arrested and jailed, which has actually happened to most of our patients. As a consequence they cultivate a life style which places a premium on avoidance, concealment, deception, and rationalization. Psychiatric interviews may produce more factual data if they are conducted in the presence of a third person who is more familiar with the patient's life than the psychiatrist. This is usually a spouse or another staff member who sees the patient on his daily visits for his methadone.

In some respects the psychiatrist's role in this program is the traditional one in an outpatient clinic setting. He sees patients for evaluation, brief psychotherapy, medication, and referral to appropriate resources for more intensive outpatient or inpatient treatment. But the psychiatrist also works with other staff members and delegates to them a great deal of the management of disturbed patients. Furthermore he must be alert to group attitudes, feelings, and interactions. Various kinds of drug addiction treatment programs may differ widely from each other, but the successful ones seem to have one outstanding trait in common—an enthusiasm by all participants for that particular program, which sometimes has the quality of religious fervor. It may be that this is an essential ingredient in the success of a program, and should be carefully nurtured both in staff and patients.

Another feature of drug addiction treatment programs is that they are often organized along family lines with a demonstrable father and mother figure (usually staff members) and child figures (usually patients). It appears that just as in real family life, this is a setting in which emotional growth and change can occur. The presence of the psychiatrist insures that these aspects of an addiction program will be learned and used.

In conclusion, it should be clear that the scope for our participation in the needs of the community is virtually limitless and that what we have so far achieved is a mere scratch on the surface. Yet it is equally clear that having embarked upon this course we are unquestionably committed to a progressively greater and even more fruitful involvement.

Some Remarks on the Psychiatry of the Subculture of Poverty

GUSTAV BYCHOWSKI, M.D.

> *Denn Armut ist ein grosser Glanz von Innen.*
> (For poverty imparts an inner glow.)
> Rainer Maria Rilke: *Das Stundenbuch*

The above quotation reflects the romantic attitude toward poverty that once characterized some of the feelings of middle-class intellectuals toward their underprivileged brothers. It hardly needs to be emphasized that it stands in stark contrast to all the political and social movements and ideologies which have developed since then as a protest against poverty. Yet it would seem that psychiatrists of the past two or three generations, owing, perhaps, to their middle-class origins, have tended by and large to ignore the psychiatric ailments of the poor, or rather, have not been sufficiently aware of the role of socioeconomic factors in the genesis of mental illness. Such a limitation in viewpoint was undoubtedly reinforced by the impact of psychoanalysis and psychoanalytic psychiatry with their inevitable emphasis on the individual psyche and its dynamics. Freud was fully aware, however, that the application of psychoanalysis to large segments of the population would necessitate modifications of psychoanalytic technique, or what he referred to as the mixing of "the gold of psychoanalysis . . . with the alloy of suggestion." The last decade, moreover, has witnessed a growing concern by psychiatrists with social issues as manifested by the rapid development of community psychiatry and the growth of psychiatric forums for the purpose of discussing and dealing with the problems of society.

At this point a semantic clarification seems in order. The term "subculture of poverty" has been introduced and used by social anthropologists, notably Oscar Lewis. It was he who, in two well-known books, *The Children of Sanchez* and *La Vida*, used this concept for the first time, to my knowledge, although earlier he had anticipated the idea in his first book, *Five Families*. The concept, as Lewis sees it, means that "poverty in modern nations is not only a state of economic deprivation, of disorganization, or of the absence of something; it is also something positive in the sense that it has a structure, a rationale, and a defense mechanism without which the poor could hardly carry on. In short, it is a way of life, remarkably stable and persistent, passed down from generation to generation along family lines." According to Lewis, "the culture of poverty has some universal characteristics which transcend regional, rural-urban, and even national differences." Such a background of extreme deprivation implies that we are dealing here not with the working class but with the so-called lower class. Indeed, according to Cohen, "the most important generative factor distinguishing the lower from the working classes seems to be the unstable employment characteristic of the lower class. In large part this accounts for their status as marginal people, always on the edge of the affluent society" (1). The concept of subculture has come of late to play an important role in sociology, anthropology, and social psychiatry. Originally used in reference to various periods and aspects of Western Civilization, it became extended to various ethnic groups, and finally to different socioeconomic groups. This latter point of view has led to important studies in psychiatric epidemiology. "The culture of poverty," writes Lewis, "is a relatively thin culture. . . . It does not provide much support or encouragement of long-range satisfaction and its encouragement of mistrust tends to magnify helplessness and isolation. Indeed, the poverty of culture is one of the crucial aspects of the culture of poverty" (2).

In this communication I propose to review briefly the sparse literature on the mental health of the poor, and to follow it by a presentation of my own data.

As will soon become evident, the consequences of severe economic and material deprivation bear certain striking similarities to those observed in emotionally deprived infants and children. As in the condition of poverty, infants and young children subjected to severe forms of human deprivation, such as Spitz showed in his classic studies on hospitalism, and to a lack of special individual care and interest, notably in the form of mothering, manifest disturbances in both mental and physical development. In fact, at an early age in the more serious cases of hospitalism it may be almost impossible to distinguish between physical debilitation and mental retardation; one might speak here of a general underdevelopment of the psychosomatic personality.

Somewhat comparable conclusions flow from the observations of Drs. Fred Brown and Ann M. Marmorale and their coworkers in the Department of Psychology at The Mount Sinai Hospital, who studied a group of first-grade elementary school children living in an economically depressed neighborhood in Harlem. In a group composed of Negro, Puerto Rican, and white children in fairly equal proportions these investigators noted severe cognitive deficiencies in visual-motor-perceptual functioning, and one-half, predominantly the same children, were below grade reading expectations. As these workers point out, a child is generally not able to read before he can achieve a certain level of maturity in visual-motor perception. The magnitude of the reading problem and the shattering impact of reading disability on future development of the child hardly needs special emphasis.

Eighty percent of the children tested were under norms in arithmetic on the Wide Range Achievement Test. Fifty-five percent of the pupils were in the lowest quartile of national norms. The Puerto Rican children performed poorly on all tests except on the human figure drawing. According to Dr. Marmorale, a possible explanation might lie in the greater emphasis placed in the lower class culture on typical male and female characteristics. On the basis of the Rorschach test, 90 percent of the Puerto Rican children might be considered emotionally disturbed. However, in contrast with the middle-class children seen in the clinic, their responses are not flamboyant. They strike the examiner as incredibly primitive, and notably poor in details. Most of the Rorschach records were dead, empty, and barren: "rocks, sticks, dead trees" etc. "You begin to wonder" observes Dr. Marmorale, "whether they live in the same world." Both the Rorschach and the Children's Apperception Test (CAT) suggest emotional isolation and alienation. Predominant are responses suggestive of emotional coldness such as ice, icicles, and snow, leading to an impression of "unbelievable emotional isolation." Anxiety and depression with the fear of abandonment are predominant. In evidence was the fear of punishment; some children were even afraid to touch the test material. Dr. Marmorale observes that these children are often afraid of their verbalization, according to the principle (apparently acquired by sad experiences) that "the less said, the better."

Studies of adolescents by other investigators show interesting differences between the affluent and the poor. The former show a more active form of passivity since they are longing to go back to a hedonistic state of existence, whereas the adolescent of poverty is pervaded by the feeling of utter hopelessness, since he has nothing in his past to long for.

A second important source of information deals with the studies of Head Start, by Drs. Douglas and Monica Bychowski Holmes. These workers were stimulated by the pioneering investigations of Martin and Cynthia Deutsch who showed that children from disadvantaged backgrounds, that is, from families below the established poverty line, suffered a significant deficit in both cognitive and interpersonal functioning. Based on a whole battery of cognitive measures, the Holmeses found that the disadvantaged five-year-olds, even after they had been through a summer of the Head Start Program, did less well than a group of three-year-old middle-class children who had never been in nursery school.

The impact of the deprivation on the total personality can be further described in terms of mood and affects, basic drives, ego-identity, super-ego and ego-ideal. (The two latter factors are obviously closely connected with the problem of sublimation.) The mood of apathetic sadness is a frequent occurrence among the poor of all the age groups, and is frequently accompanied by sullenness. These observations confirm the data of other workers. For example, Kozol, in his *Death at an Early Age* describes "the destruction of the hearts and minds" (3) of Negro children in the Boston Public School, and presents us with sharp etchings of the patterns of self-blame which the children had introjected from their oppressive environment. "There were also children who did not give in at all. It was not these—not the defiant ones—but the children who gave in to their teachers most easily and utterly who seemed the saddest." A pathetic illustration is provided by a little girl who barely escaped having her skull fractured by a blackboard which collapsed during a lesson in that decrepit school. "The girl whose desk was underneath the blackboard now had the most curious expression on her face. I couldn't tell whether it was simply the look of being numb or whether she was not, like so many other of the children in this building, getting herself set up for the introjected ritual of blaming herself." Here the belief in inferiority is the result of interaction between the oppressed and the oppressor.

Observers point out that the children of poverty learn at an early age that the best way to stay out of trouble is to keep quiet. It is this attitude at an interview which makes them appear dumb and sullen as a protective defense against a possible assailant or an enemy, represented by the interviewing member of the establishment. Other observers confirm the assertion that depression is a frequent clinical finding among the poor. According to S. M. Miller, the dispossessed suffer from the feeling of chronic dependence; their life moves from one crisis to another. The feeling of insecurity and the lack of hope in the future are characteristic of those who are not firmly anchored in the economic system of the society (4). Unfortunately, this applies not only to the dispossessed and the declassé, in the sense of Marx, but also to some factory workers. Kornhauser writes in his study of the mental health of Detroit factory workers that "what is important is everything that deprives the individual of purpose and zest, that leaves him with negative self-feelings, anxieties, tensions, a sense of lostness and futility which distorts his thinking and obstructs effective behavior" (5).

In a study on sociocultural aspects of depression, Schwab et al came to the conclusion that "the affective symptoms of dissatisfaction, self-accusation, and hopelessness correspond with the findings of the Midtown Manhattan Study which indicate that lower social persons experience feelings of futility to a significant degree" (6). Haggstrom makes the point that it is helplessness which is the dominant factor shaping the personality of the poor. The result is a situation of dependency and powerlessness through internal personality characteristics as well as through social position. "This leads to apathy, hopelessness, conviction of the inability to act successfully, failure to develop skills, and so on" (7).

The image of the self which obtains under these circumstances is indeed a poor one. "The shame that frequently accompanies limited opportunity for mastery often leads to heightened hostile aggressiveness and the destruction of trust in others. Living in poverty inevitably leads to questions about one's own adequacy as well as about the values of society. The 'brave front' often seen is a protection against the core of depression that is a natural consequence of living under these conditions. The constant exposure to betrayal of confidence by others adds to the feelings of shame as the individual recognizes that he has built his confidence upon false assumptions. Anticipation of love and happiness which is not fulfilled furthers self-debasement" (8).

Chronic deprivation resulting in frustration of elementary needs with no hope of improvement seems to lead to further changes in personality. It should be borne in mind that in conditions of extreme deprivation two basic ways of dealing with elementary needs or instinctual drives are available to the individual. The first is renunciation—isolation or repression; the second consists of an aggressive gesture aimed at the attainment of some immediate, even if only substitutive, gratification. The former may be expected to lead to apathy, withdrawal of affect, and to alienation; the latter to acting-out as manifested by psychopathy, violence, destructiveness, and so on. We can watch them, as it were, in statu nascendi in children and young adolescents, and in a solidified form in adults.

Examples of these manifestations are provided by patients at The Mount Sinai Hospital. These observations were obtained from: a) A group of patients observed either by myself or by my colleagues, and b) A small group of children in the Childrens' Clinic.* These observations are drawn by and large, though not exclusively, from the two ethnic minority groups predominant in New York City. It can be safely assumed that some trends and factors are related rather to the ethnic origins than to the socioeconomic situation. Yet, it does not seem always possible to differentiate between both sources (9).

Fernando M., age 9 is the last but one in a family of seven living in typical crowded Harlem quarters. The father's small income is supplemented by welfare. There is a great deal of fighting between the children. Fernando has been sent away from school on several occasions for bad behavior, but he apparently responded favorably when he was changed to a less strict teacher. During the interview he was sullen and uncommunicative; when asked what he would like to be in the future, he responded without hesitation, "A bum." "What would he be doing?" He answered, "Drinking." "Where would he get the money?" He answered, "Sacando" (robbing).

José V., age 12, is one of a family of 11. The mother comes to the clinic with the boy, and explains that she is "punishing her husband for his misdeeds." She describes him as an angry man who hits the children. The father himself was one of a family of 11, who came to New York from the mountains and returned later in utter frustration to Puerto Rico. The family lives on relief in great poverty. José had been seen in the Department of Pediatrics of The Mount Sinai Hospital where he was treated for malnutrition, anemia, and hookworm infestation. His behavior was described as uncooperative and negativistic. Recently he has suffered from an acute psychotic episode which was diagnosed as a dissociative reaction or psychomotor epilepsy. He screams at night, and has fallen out of bed. José looks unhappy and speaks very little during the interview. He denies hallucinations. He says he thinks of his papa and is vaguely afraid—"tengo miedo"—but he does not elaborate.

In the family history of these children it is not always possible to disentangle the influence of extreme material deprivation from the loose or otherwise unfavorable family structure. The latter factor may contribute as much or even more to the feeling of insecurity, depression and diffusion of ego-identity. We have seen a number of children coming from homes where the economic situation was far from desperate but where some of the typical family disruptions had occurred, leaving, so it seems, scars on the personality of the child.

Milda H., age 11, is tense, has angry spells, and tends to become uncommunicative. She lives with her father and stepmother. Her mother and three siblings remained in Puerto Rico while her mother sent her here to live with the father in the hope that it would make things easier for the child as well as for herself. The stepmother has three children from a former husband. (Incidentally, it seems that neither of the couples got a divorce from the former marriage.) The mother and her children in Puerto Rico are on welfare. Milda is unhappy here, the climate is cold and her stepmother keeps her indoors. Milda is not sure whether her father cares for her. He does not work but his present wife is contented: even when living on welfare, she has it better here than in Puerto Rico.

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*I wish to express my thanks to my younger colleagues from Mount Sinai Staff who helped me in the collection of the clinical data: Dr. Rita Wallsh in the collection of adult case histories, and Dr. Henry Vassallo in the observations in the Children's Clinic.

Sharon D., a Negro, was hospitalized in the Department of Psychiatry at the age of 16. The family lives mainly on welfare; the father works only sporadically, and drinks. In crowded quarters the patient lives with her parents, five siblings, and a married sister who moved in with the family since her husband did not want to pay any rent. Often there was no money. When Sharon came home from school, there was seldom enough food in the icebox.

At the age of 12, Sharon started to have fantasies and to imagine things she might be doing. "I started pretending and making believe that I can do and will do things—that's all I had." She stopped learning at school at the age of 14. She felt lonely. She had no friends but she made herself believe that she had them. She allowed boys to take liberties with her so that they would like her better. She envied other girls for having boy friends. She believed her mother was tired of her. Her father drank, and was rude and assaultive. Sharon claims that at the age of 6 she was raped by an uncle; however, her older sister denies it. . . . One evening when she felt more lonely than ever, she went out alone at midnight to a city square where she saw other girls playing with boys. A car drove up and a fat white man got out, talked to her, and invited her for a ride. He had intercourse with her in the car and let her out. She got pregnant and had a normal delivery. She was hospitalized because of her bizarre behavior. "The baby is all I have", she says. Yet, remembering that at the age of 12 she had killed a little kitten, now she is afraid that she might do the same thing to her child. It is evident that her fantasy life developed as an expression of her need to fill the emptiness of her world, so devoid of real feelings and happenings. Quite naturally, this original fantasizing developed into a whole imaginary world taking her further away into an autistic withdrawal. It is also clear that her sexual escapade originated in the same feelings of void and alienation, in the search for some excitement which would relieve the hopeless monotony of her existence.

Even in conditions of relative family stability, the climate of economic frustration is often combined with emotional deprivation, indifference, hostility, and lack of adequate models for identification. These configurations lead to a poor, blurred formation of ego-identity and ego-ideal. However, the conditions become even less favorable when, as so often happens, the family structure is disrupted and both maternal and paternal figures change in rapid succession often with one of the parents missing permanently or intermittently. It must be acknowledged in any case that a careful examination of the clinical material demonstrates clearly the methodological difficulty in establishing a direct causal connection in every instance between economic deprivation and psychopathology. In my own limited observations of patients from a background of affluence, for example, I have seen clinical pictures not unlike those described above, compounded of a mild depression based on low self-esteem, a feeling of emotional deprivation, some degree of alienation, a certain emotional flatness, and a good deal of outer- as well as inner-directed aggression. Despite these observations, we can speak with some confidence of the probability that certain symptoms and syndromes tend to occur far more frequently, and with some special coloring, under conditions of poverty. There can be little doubt that poverty represents an important and an ominous cause for a general sense of deprivation and as such may contribute to the stunting and thwarting of personality. Extreme material deprivation combined, as it frequently is, with a deficient parental nurturing, contributes to that lack of basic trust which is essential for the growth of a strong and clearly delineated ego. The lack of good parental models (introjects) means that the world, or reality as such, is viewed as unattractive, or even ominous and frightening: the latter is more likely to be the case, the more "bad" introjects take the place of good internalized parental images.

In light of these observations concerning the psychiatric implications of poverty we should insist upon a determined and decisive break with the denying or ignoring attitudes towards these problems in the past. To quote a recent writing on the subject: "To say that the poor have been controlled as objects by opponents is to say that the poor have been living in an underworld, in a collective unconscious, kept out of sight of the majority population except in distorted and virtually unrecognizable representations. Like other groups held in the collective unconscious, the poor, as a force, are disguised, appearing in forms as strange as those impulses which appear from the personal unconscious in the form of dreams, symptoms, or humor" (10).

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The Teaching Program of the Department of Psychiatry for Medical Students

MARCEL HEIMAN, M.D.

Attempting to describe the teaching program for medical students at the Mount Sinai School of Medicine at a time when we are finishing the second year of its existence confronts us with the choice of describing what we have today, what tomorrow may bring, or what we hope for in the future. I shall attempt to combine all three and start out with the aim as visualized at the time when our medical school was in the planning stage.

The goal of the comprehensive teaching program of psychiatry is based on the Mount Sinai Medical School Concept and on the concept to which the Department of Psychiatry of The Mount Sinai Hospital has been dedicated since Dr. M. Ralph Kaufman first became its Director. The Mount Sinai Concept is a theoretical proposition aimed at an ideal—perhaps even utopian—goal. One starts out with excellent students selected according to standard medical school admission rules and one gives them the best possible education in the science of medicine while guiding them by teaching and precept to remain humane and compassionate persons.

This intertwining of scientific excellence with compassion finds its complement in the manner in which the Department of Psychiatry has been carrying out its program of treatment, teaching, and research within the hospital long before the establishment of the medical school. It has been carried out through an elaborate liaison service affiliated with every inpatient and outpatient department—in which each generation of young interns and residents, as well as members of the Attending Staff have been exposed to the characteristic approach of the psychiatrist to sick people—an approach which is often radically different from that of other physicians.

Would it not then appear that the Department of Psychiatry might be quite useful in the implementation of the Mount Sinai Concept? Might it not be desirable to have members of the Department of Psychiatry participate wherever possible in teaching exercises throughout the medical school? Could this not be the most effective way of helping the student gradually develop the concept of interaction between physiological and psychological forces?

While it would be desirable to introduce the first-year student to a living human being who suffers and thinks and feels, and while it might be appropriate to invite a psychiatrist to comment on these manifestations, we have not reached that point yet. Currently during the first year, one psychiatrist is assigned to the Department of Physiology and one to Pharmacology, where the teaching program permits the psychiatrist to demonstrate such issues as body–mind unity and patient–doctor interaction. Psychiatrists are also assigned to the organ system teaching program during the latter part of the first year, i.e., neurosciences and cardiovascular-respiratory system, where patients are used for teaching purposes.

During his second year the medical student is initiated into clinical psychiatry, notably through the "Introduction to Comprehensive Medicine," a 30-hour course extending over an eight-week period, pertaining to the total evaluation of the patient. This course starts with learning the essentials of psychiatric history-taking and of the mental status. The major portion, however is devoted to didactic teaching and to the demonstration of patients to larger groups of students. The actual interviewing is carried out in smaller groups. It is the intent of this course to help the student perceive health and illness within the context of normal growth and development and to sensitize him to the social and psychological, as well as to the biological determinants, of health and illness. The student is also made aware of the various modalities that are available for the prevention and treatment of mental disorders.

The third-year curriculum offers the opportunity to reinforce this approach through weekly seminars in every clinical division and in every area of combined clinical teaching. We have a highly developed liaison psychiatry service which is engaged in the teaching of many aspects of psychiatry as it applies to the everyday practice of the nonpsychiatric physician. Working with colleagues from other departments, these psychiatrist-teachers conduct joint exercises demonstrating the role of the psyche in all aspects of illness and showing how this knowledge can be used to help the patient and his family. These exercises are held on the clinical service in which the student is serving his clerkship.

At the time of writing the students who began their medical education in September, 1968, have finished their second year and will have their clinical clerkship during the ensuing one. A description of the clinical clerkship in psychiatry is now in order.

Clerkship

Although the Mount Sinai School of Medicine is now only in its second year, the teaching program for the psychiatry clerkship has already undergone a number of changes. Consider the complex structure of the program: it has to be substantial throughout and yet open on both ends so as to be responsive to the needs of the students and to the expectations of the faculty. Like a topological object, however much any one part is changed, its relationship to all other parts of the structure remains unchanged.

In addition, the clerkship must be integrated into the four-year curriculum of psychiatric teaching of which it is an essential part. Modifications in the preclinical teaching schedule affect the clerkship program. For instance, as soon as the teaching of psychiatric history-taking and the technique of mental examination became assigned to the second year these subjects could be dropped from the third-year clerkship curriculum and replaced by clinical work. Similar reasoning applies to the teaching of "growth and development" which, seen as psychiatry's basic science should be taught during the preclinical years. Once this is established it will be possible to eliminate the teaching of "growth and development," the most time-consuming part of the didactic program of the clinical clerkship, to make room again for clinical work.

The clerkship in psychiatry is planned to contain the essentials of psychiatry for every physician. This is in contrast to the electives to be described later.

During their psychiatric clerkship, the students, in groups of 12, spend four weeks in our department, where the four adult inpatient units are their base of operation. Emphasis is placed on clinical experience.

Acknowledging and supporting the need of the students to participate actively in clinical work with patients to the extent of their ability, the students, in rotation, spend evenings and nights in the department. This time, much less structured than the rest of the clerkship, has been found most rewarding as a learning experience by both students and faculty.

During these hours, the students are assigned to the resident-on-call, accompanying him through every part of the hospital where a psychiatrist is needed. By sleeping in the same quarters as the resident, getting up with him to answer a call, and other similar duties, the student experiences what "psychiatric first aid" is all about and what it can accomplish.

The aim of the clerkship is to enable the student to learn the principles of psychiatry as a discipline. Towards that aim the teaching encompasses an understanding of aspects of behavior, personality and character traits—as well as the importance of the knowledge of the biological roots of psychologic manifestations. The final goal is a holistic approach: to see and understand the "total" person.

However, there is an additional aspect of psychiatry stressed both in clinical seminars and clinical conferences, that is, the relationship of psychiatry to medicine as a whole and to the various medical specialties. (This relationship is also being taught by members of the Department of Psychiatry to the students during their clerkship in medicine, surgery, pediatrics, and obstetrics and gynecology, but perhaps somewhat modified to convey the point of view of that particular specialty.) What we are aiming for—especially for those students who will not choose psychiatry as a career—is a deeper awareness that an understanding of the psychological aspects of symptoms, of disease processes and of various therapeutic modalities, not only offers a useful "operational" approach to medicine regardless of the field in which the student will later work, but constitutes the best and most sophisticated approach to the practice of medicine.

The clerkship aims to acquaint the students with the wide range of psychiatric illness from childhood to old age; to reveal the spectrum of psychiatric treatment extending from the Emergency Room interview to slow-paced psychotherapy and including those intermediate combinations of therapies utilizing groups, drugs and electroshock; and finally to introduce the various types of treatment facilities, e.g. inpatient, outpatient, partial hospitalization, long-term custodial care and so forth. The clerkship offers the student an opportunity of seeing the psychiatric patient not only as a troubled individual but also as a member of a community with which he establishes a mutual interaction, be it a family, the ward setting etc.

The teaching staff engaged in this program is composed of approximately 40 members of the Department of Psychiatry at The Mount Sinai Hospital and the institutions affiliated with the Mount Sinai School of Medicine: Beth Israel Hospital, Elmhurst Hospital, and Manhattan State Hospital, plus individuals attached to the auxiliary disciplines—psychology, social work, psychiatric nursing, sociology and occupational therapy.

When the student commences his psychiatric clerkship, he has already been instructed in the essentials of taking a psychiatric history. Now, his skill has to be sharpened. Aided by the supervision of a preceptor the student must learn special techniques of interviewing and particularly how to elicit the relevant data in the lives of the patients assigned to him. He also will have to gain a better understanding of the patient–physician relationship and how this affects both participants. Finally, he will have to become sensitive to the patient's behavior and to its viscissitudes; in addition, hopefully, he will become attuned to subtle changes in the patient's mood. These complex data are all used as aids in arriving at a clinical diagnosis.

In addition to preceptor teaching we have recently established a tutorial program in which senior attending psychiatrists met with two or three students at regular intervals during the clerkship in an informal and unstructured way in order to discuss whatever questions, problems or perplexities may have arisen in the minds of the students.

Aside from his work with patients and the time assigned for preceptor and tutorial sessions, throughout the clerkship the student attends seminars and conferences which are centered about clinical material. Since no more than one such meeting takes place on any given day, the major available time is spent with patients. An enumeration of the subjects covered during these meetings best conveys an idea of the broad spectrum of the instruction offered: 1. Eight Unit or Ward Conferences. These are conducted by the Attending Psychiatrist in charge of the Unit and are attended by all Unit personnel. 2. Six Clinical Conferences. Here the students present their work with patients to senior members of the Faculty. 3. Five Seminars with clinical demonstrations: Child, Adolescence, Geriatric, Medicine, Neurology. 4. Four Seminars with clinical demonstrations on Phenomenology and Interviewing. 5. Three Seminars devoted to Depression and Suicide, and pharmacotherapy. 6. A film on Mother-Infant Interaction. 7. Psychological Testing. 8. Partial Hospitalization. 9. The Outpatient Department. 10. An Introduction to Hypnosis.

Teaching during the four-week clerkship is rounded out by a visit to some of our affiliated institutions—Beth Israel, Elmhurst, and Manhattan State Hospitals, for exposure to those aspects of psychiatry not available at Mount Sinai Hospital, such as, treatment of drug addiction, acute psychotic patients, and chronic psychotic patients.

Electives

While the students have limited time available for electives during the first and second years, the entire summer following these two years may be used as elective time.

The elective courses for which time is allowed during the first and second years are necessarily limited to (1) areas related to basic sciences, and (2) areas related to medicine, in which the student may have an opportunity of broadening this general perspective.

Basic science as it applies to psychiatry should be understood as everything fundamental to the understanding of clinical psychiatry; for instance, growth and development, psychopathology. The latter has already been included in the elective program for the second year and it has proven to be quite successful.

During the first year of the medical school (1968 9), a fair number of our first-year students showed an interest in psychiatry. In response to their desire to know what psychiatry is all about we set up two electives—one, a theoretical seminar, "The Role of Psychiatry and the Psychiatrist," where one of the Senior Attendings met with the students, and the other a practical one, inviting the students to attend the Unit Conferences. Their expressed interest in the "Basic Writings of Freud" was met through a Reading Seminar.

During the summer however, the first- and second-year students are not restricted as to content of elective courses. In 1969, our first venture in setting up a summer elective program, there were 12 students taking electives in clinical psychiatry (eight in adult, two in adolescent, and two in child psychiatry) while one student selected one of the four electives offered in Research, namely, Suicide Research. All the 13 students accepted for the 1970 summer electives were interested in various aspects of clinical psychiatry. Compared with the first summer, the 1970 program had been planned and structured in greater detail. For the first time, Beth Israel and Elmhurst hospitals participated in our summer fellowship program: two students did their clinical work at Elmhurst Hospital, while four were assigned to The Mount Sinai Hospital and to Beth Israel Hospital. In addition, one student worked in child psychiatry. The above 11 students have completed their first or second year. Two third-year students were assigned to the Emergency Room, the Outpatient Department, and the Liaison Service. Six of the thirteen students came from other medical schools (Downstate (two), Rutgers, Yale, Connecticut, Oregon).

Each student in the Electives Program is assigned to a preceptor who supervises his clinical work which depends on his level of experience and application to the field. All 13 students take part in the didactic seminars which have been set up for them. A senior faculty member, assisted by a junior member, is in charge of the whole program, supervising the clinic work and assuming responsibility for the seminars.

During the academic year 1969 70 we offered our second-year class 15 electives, of which the following four were chosen and were attended by 20 students: a Seminar in Psychopathology and Clinical Psychiatry; Emergency Room Liaison Psychiatry; General and Specific Aspects of Psychiatric Practice, and Psychological Problems of the Creative Personality.

During the same academic year, we offered our fourth-year class 32 electives. Fourth-year students had more than six months of the year available for elective time. All five institutions affiliated with the Mount Sinai School of Medicine participated, offering between one (Manhattan State Hospital) and

18 (The Mount Sinai Hospital) subjects. The students were interested in clinical studies, spending from four to eight weeks in various parts of our department.

Altogether, we offered 58 electives to our students. There is quite a discrepancy between this figure and the small number of electives chosen. It needs to be noted, however, that the planning of our electives is geared to a student body of 400 anticipated three years hence.

Electives are also prepared by the Department of Psychiatry in conjunction with other Departments. For example, upon the specific request of a student who is planning to become a surgeon and who is interested in the psychiatric problems of surgical patients, a special elective was prepared. He was assigned to a senior liaison psychiatrist whom he accompanied on the surgical wards, where he participated actively in every aspect of the liaison work, resulting in a very satisfactory learning experience.

More than any other department of our medical school, Community Medicine shares many of the interests of the Department of Psychiatry. Since a large number of our students wish to gain a better understanding of the interaction between social and psychological forces, combined electives by the Departments of Psychiatry and Community Medicine are a logical answer. These electives also express the desire of our department to provide a broad exposure for the student to the pressing and vexing problems of the society in which he lives: violence, crime, poverty, drug use, and the psychiatric complications attending them.

Electives may assist the student in exploring not only the proximate community and our own subcultures, but those of other parts of the world. During the past year we set up two electives as diverse as a mental hospital in England and a community project on Africa's west coast.

Some Thoughts for the Future

Clerkship

Since September, 1968, when the Mount Sinai School of Medicine commenced its teaching, six groups of students had a psychiatric clerkship: the first three groups for two weeks, the last three groups for four weeks. As a result of the observations by the faculty and the constant feedback from students during and at the end of the clerkship, we have been changing and modifying the curriculum of the clerkship. Our aim is very clear: we want the clerkship to be as total a clinical experience for the student as we can possibly make it. Such an objective can be achieved only if the psychiatric teaching during the preclinical years is structured and organized to serve this purpose, that is, to prepare the student for working with patients. We hope that in another year we shall have completed the integration of a four-year psychiatric curriculum in accordance with the above plan.

Electives

Compared with the clerkship it is much more difficult to implement the objectives of our elective program. There are several reasons for this. While the clerkship represents in essence what we consider a core curriculum, the electives by their very nature transcend any such rigid concept. Electives necessarily must either amplify what could only be touched upon during the clerkship or they offer the students the opportunity to work in special areas of psychiatry and in areas combining psychiatry with other medical fields or with non-medical fields. Such combined electives may take the student to other local institutions and even to other parts of the world. Another difficulty in planning for and structuring an elective program lies in the fact that, compared with clerkship students, those for whom the electives are designed are a relatively heterogeneous group. The electives should respond to the needs and interests of students of all levels, and they should stimulate interest as well as satisfy it. They have to be sensitively attuned to social changes, both in the community and in the world at large. Consequently it is desirable to have an openended elective program in order to assure its flexibility.

In closing, I wish to express the hope that the teaching program of the Department of Psychiatry for our medical students will be carried out with an excellence equal to the proud tradition of the Department.

The Residency Training Program

DAVID KAIRYS, M.D.

It has been observed that if one studies the way in which a society rears its children, one may hope to learn a great deal about that society's goals and values. Similarly, the study of its residency training program is a good vantage point from which to observe the aims and ideals of a hospital department. The Department of Psychiatry at The Mount Sinai Hospital in many ways exemplifies the development of psychiatric services in post-World War II America. At the same time the department bears the indelible stamp of its Director, Dr. M. Ralph Kaufman, so that in relating the way in which it has trained its residents, I will inevitably be reflecting the spirit of the man who founded the department and brought it to its present stage of development.

In describing our training program I cannot pretend to be an objective observer, since I have been a member of Dr. Kaufman's staff almost since he arrived on the scene, and for almost a decade I have been entrusted with the responsibility of directing the program. What follows, therefore, will necessarily be a view from within.

The Philosophy of the Department

It is important for an understanding of the conduct of the training program to explain something of the philosophy which underlies it. Like the chiefs of many other major departments of psychiatry in this country, which grew up in the years after World War II, Dr. Kaufman is a psychoanalyst. He was for many years a leader in the field of psychoanalysis and held major offices in its national organization. Inevitably the staff that he attracted has included a great many psychiatrists who were similarly trained in psychoanalysis, although this has never been, in any sense, a criterion for appointment to the staff or promotion within it. In a staff that numbers about 150 psychiatrists, almost one-third, including most of the Senior Staff, are psychoanalysts. This numerical fact is crucial to the nature of the department and its training program, and to clarify its significance it is necessary to say something about the relationship between psychoanalysis and general psychiatry.

Sigmund Freud, the man who founded psychoanalysis, long ago gave it a tripartite definition: (1) A set of hypotheses explaining human behavior and personality in both health and disease; (2) A specialized technique for the treatment of some forms of emotional illness; (3) A method of research in human personality functioning. It is the first part of this triple definition which is relevant here. Psychoanalytic theory, as conceived by Freud, and elaborated and extended by his students, has become a general theory of personality. It is widely accepted that analytic theory has the greatest explanatory power of any set of hypotheses yet devised in the area of human behavior.

During and after World War II a great many American psychiatrists came to see the enormous value of psychoanalytic concepts in the understanding and management of psychiatric disorders. What resulted was a marriage of clinical psychiatry with psychoanalytic theory and out of that marriage has issued an approach to mental illness which has come to be known as "psychoanalytically oriented" or "dynamic" psychiatry. Dynamic psychiatry has been the major force in American psychiatry for the past quarter of a century. Psychoanalysts came to be in great demand as directors and attendings in hospital departments of psychiatry as well as in medical schools, and many major departments, as I have indicated, have long been headed by analysts and have included analysts on their staffs. Departments staffed in this way have taken the lead in teaching dynamic psychiatry to their residents; but even departments whose staffs included no psychoanalytically-trained psychiatrists have often based their teaching on "dynamic" concepts of human personality.

While it is impossible in this essay to enter into an exposition of psychoanalytic theory, some of its crucial assumptions should be mentioned, to enable the non-psychiatrist reader to understand better the content of a "dynamic" training program.

For our purposes, I would list five hypotheses as being basic to all psychoanalytic theory; they have long since been verified by a mass of clinical and research data. (1) Crucial segments of human mental and emotional functioning go on below the level of conscious awareness, i.e., they are unconscious. These unconscious processes play a critical role in motivating human behavior. Hence, while man has been called a rational animal, much of what he feels and thinks is determined by unconscious, irrational forces of which he is not aware. (2) The experiences of the early years of an individual's life lay the foundation for his future development; the details of childhood development are profoundly important variables in the understanding of the adult personality, both in health and disease.* (3) Human behavior is not random, but is largely determined, so that it is possible to trace causal links in a course of action or the development of an illness. (4) Conflict plays an important role in human personality: conflict between one's impulses and one's conscience, between impulses and the need to maintain equilibrium and adaptation, conflict between one's inner life and the demands of the external world. (5) Human beings have a remarkable capacity to transfer onto others attitudes and emotions they have felt for the key individuals of their earliest years, notably, their parents and siblings. This capacity, the phenomenon of "transference," plays a great role in human affairs generally, but in particular has proven to be a powerful therapeutic tool not only in psychoanalytic and psychotherapeutic treatments but in the practice of medicine in general.

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* The primacy of the influence of the early years has sometimes been construed to mean that subsequent influences, experiences or events play no significant part in shaping the personality, determining emotional development, or affecting mental health. This is obviously erroneous for otherwise it would be difficult to account for the far reaching changes that can be effected by psychoanalytic treatment, to say nothing of the modifications that may take place through less ambitious therapies or even through the impact of life events.

While placing great emphasis on the impact of the immediate environment (parents, other adults, siblings), on the developing human organism, psychoanalytic theory at the same time assumes that genetic endowment also plays a large role, nor does it neglect the importance of cultural and social influences as yet another set of determinants. In the end, the personality and behavior of any individual is seen as the sum of the complex interplay of genetic, psychologic, cultural, and social factors, so that man is viewed as a bio-psycho-social organism.

Given sufficient data, the theoretical system elaborated from these assumptions has the potential for explaining a very wide range of phenomena in the field of human behavior, and not the least in the field of clinical psychiatry. Consistent with his own basic training in the psychoanalytic discipline, Dr. Kaufman has insisted on viewing all innovations in psychiatric therapy, for example, including the so-called organic therapies, within the context of the principles of psychodynamics. Indeed, while in our own department a wide range of therapeutic modalities are employed, the choice of modality, the observation of its effects, and the particular clinical problem involved are viewed within this theoretical framework. The psychoanalytic theory of personality forms the underlying philosophy of "dynamic" departments of psychiatry, and the training program at Mount Sinai as Dr. Kaufman has developed it is no exception.

But beyond this conceptual framework there are other aspects of the philosophical implications of a dynamic, or "psychoanalytically-oriented" training program which should be mentioned.

Psychiatrists who are fully aware of the great power exerted by unconscious processes in the lives of human beings have a special regard for the manifestations of these processes. Rationality in human affairs is without question usually a desirable end; yet at the same time we know that much that lends beauty and color to human existence proceeds from the less rational, unconscious area of the psyche, like great works of art, music, and the writings of poets, playwrights and novelists. The transporting experience of being "in love" is in its essence irrational and is nurtured by unconscious forces. Even the brilliant "inspirations" that produce new and elegant scientific hypotheses apparently have sometimes resulted from a blend of the highest level of rational thinking with obscure elements derived from the unconscious mind. For the analytically trained psychiatrist, then, the simple equations—"rational = good" and "irrational = bad"—do not hold. The irrational aspects of human life are heavily involved, it is true, in mental illness and in human suffering of all kinds; but these phenomena must also be respected for the endless ways in which they enrich man's existence. While this view may not often be encountered in other branches of medicine, it must pervade the atmosphere of a psychiatric training program that seeks to teach the complexities of human mental life. In the Department of Psychiatry at Mount Sinai Hospital the residents are exposed to this concept throughout their training.

Closely related to this view is an abiding respect for the uniqueness of every individual human being. One who works every day with the endlessly variegated manifestations of human emotions knows that people cannot be put into neatly labelled categories. Regardless of the broad similarities that can be seen within various syndromes of emotional disturbance, we know that each individual suffering from a defineable disorder is still very different from every other individual who is given the same diagnostic label. The admonition that "no two patients are alike" is repeated endlessly in the teaching of residents; cliché or not, it expresses a far-reaching truth. It means, for example, that it is the therapist's task not to lead his patients to achieve his own preconceived norm of behavior, but rather to help each individual attain that degree of achievement and satisfaction of which he alone is uniquely capable.

From this regard for human individuality there proceeds another trait which typifies the psychoanalyst's approach to his patients, and to human beings in general—namely, a tolerance for behavior which, while harmful to no one, is nevertheless conspicuously different from that which is considered conventionally acceptable. The analyst devotes many hours to painful self-scrutiny in the course of the personal analysis which forms part of his professional training. He learns, once and for all, hopefully, that the conflicts which bedevil the suffering patient have their counterparts, if only in embryonal form, in himself as well as in most of all mankind. The strange visions of our own dreams are not very different from the waking thoughts and speech of the schizophrenic; the murderer, the exhibitionist, the suicide—who are they but individuals who yield to impulses which "normal" people harbor in well-controlled and disguised forms? This knowledge of the commonality of psychic conflict should engender great humility and discourage the tendency to feel condescension or a sense of superiority toward those whose behavior is considered "deviant." "*Nihil humani alienum a me puto*"—"I consider nothing human as alien to me"—provides a concise statement of the tolerance essential to a profession whose ideal is to relieve, rather than to condemn, the sufferings of the psychically ill.

We live in an era which seems to be marked by an erosion of human values and by a disappearance of individual identity. Human affairs are conducted by increasingly larger organizational structures which have become progressively more impersonal and more removed from contact with those whose lives they affect. The miracle of the computer, with all its incredible potential for speed and efficiency, at the same time contributes to the seemingly inexorable process of de-humanization. Even the practice of medicine, an undertaking in which the personal contact of the sick with the healer has always been a sine qua non, is witnessing mechanized and computerized developments which, if not properly channeled, may in time erode the basic humanity which is not only one of medicine's noblest traits, but is an indispensable keystone in the therapeutic process.

In the midst of this frightening tide of depersonalization, psychoanalytic psychiatry stands as an emblem of man's personal involvement with mankind, a champion of the dignity of the individual, a spokesman for tolerance of non-conformity, and a proponent for the pursuit of the fullest potential of individual aspiration.

The philosophy I have outlined above is immanent in the thinking and feeling of a "dynamic" psychiatrist; by the same token inevitably it becomes the point of view of a "dynamic" department of psychiatry and hence the epitome of what it teaches its trainees, sometimes explicitly, sometimes by unspoken example and precept. The ideas briefly sketched in the foregoing have been given full expression in the content and structure of the residency training program that has evolved under Dr. Kaufman's direction.

Design of the Training Program

It is not my intention to describe our training program in the kind of detail that might be suitable for a departmental brochure. My purpose, rather, will be to indicate how the ideas outlined above have been carried into practice.

Supervision as a Form of Teaching

The actual treatment of patients under the direct guidance of a teacher forms the backbone of house-staff training in virtually all medical specialties. Psychiatry is no exception to this, but the nature of psychotherapy has necessitated the development of a special kind of "guidance." The internist can listen to a heart along with a resident; the surgeon can stand by while a beginner learns to do an appendectomy; but psychotherapy does not prosper when someone other than the doctor and his patient participates in the therapeutic sessions. Instead, borrowing a pedagogical device developed for the training of psychoanalysts, psychiatry utilizes a system of supervision which enables the resident to report his day-by-day therapeutic sessions with his patient in as much detail as possible. The supervisor—whose title in our Department is "preceptor"—uses the material of this report to discuss the resident's management of the session or sessions, often going into great detail to teach various aspects of the technique of therapy. At the same time many other issues may be discussed—the historical evolution of the patient's difficulties, the form of his unconscious conflicts, the nature of the symptomatology, diagnosis, and prognosis as well as broad related problems in psychiatry illustrated by the case under discussion, and so on. In addition, the resident's own reactions to his patient's behavior may become an important subject for discussion. The supervisory hours thus become a forum not only for the discussion of the resident's handling of his patient, but for any aspect of psychiatry that may be relevant. It is not surprising that residents are often of the opinion that their most basic learning has occurred in their individual sessions with patients and in the subsequent discussion of these sessions with the preceptor. Despite the theoretical knowledge that a resident may gain from reading or from seminars and conferences, his "moment of truth" comes when, closeted with a patient, he must learn to deal spontaneously with the complex problems of a distressed human being who turns to him for help. It is in the fire of this one-to-one relationship, which the resident lives through as it happens and scrutinizes later with the critical help of a preceptor, that the skills of a psychiatrist are best developed.

The preceptorial relationship has, in addition, a teaching function which goes beyond the formal content of what is explicitly discussed. In the course of many successive hours spent with a resident, a preceptor will inevitably reveal much in the way of attitudes, opinions, ethical values, philosophical viewpoints, and so on, which the resident will absorb even when they are not specifically articulated. As in any teacher–student relationship, a great deal of what is learned depends upon the student's identifying himself with his teacher whom he takes as a model and from whom he takes on, often without realizing it, mannerisms, attitudes, and professional "style." Psychotherapy as an art and the scientific hypotheses upon which it is based can best be taught in the close, individualized teaching of the preceptorial relationship.

The critical importance of this form of teaching in psychiatry is widely recognized, but Dr. Kaufman has developed it to a degree which has made his department unique. While it is a common practice in some institutions to assign the work of supervision to junior staff and even to senior residents, he has insisted that this difficult form of teaching should be a function of seasoned practitioners. At the same time he has aimed at a high intensity of supervision, specifically the allocation of an hour of "preceptor time" per week for each of the resident's patients—a ratio which is unusual outside The Mount Sinai Hospital. This has necessitated the recruiting of a large corps of preceptors, but attracting and keeping a dedicated staff has been one of Dr. Kaufman's great talents. Indeed during the eight years since the Department expanded into its new building, the number of attendings holding the rank of Preceptor or carrying out the preceptorial function has grown enormously. This large mass of teaching talent is applied to a total of 22 residents making up the 1st and 2nd year groups, with a small number of preceptors assigned to outpatient work with the third year residents.

A concomitant requirement for the maintenance of this level of supervisory teaching is that the residents' case loads be kept small. With a normal complement of four to five residents for each 24-bed inpatient unit, a resident's case load, under optimal conditions, averages around six patients. This ratio, regarded by outside observers as a great luxury, not only increases the possibility of providing good patient care, but at the same time offers optimal teaching possibilities. It enables the resident to study patients carefully and in depth, and makes it possible to provide the kind of supervisory experience just described.

The intensive treatment of patients on an individual basis through verbal psychotherapy is by no means all that our residents learn in the course of their training, as will be made clear; but learning to do psychotherapy is central to much else that the residents learn. It has been our conviction that to work closely with a patient over a period of time is the best way in which to learn basic psychiatry—beginning with careful observation and description of phenomenology, going on to understand the forces that have produced an illness, and learning how to deal with those forces in ways that may be reparative.*

The Inpatient Unit as a Teaching Forum

Concentrated work on an inpatient unit (this includes a rotation for some six months through the Day and Night Center), which occupies our residents for the better part of their first two years, brings into play many essential skills beyond those acquired in learning individual psychotherapy.

An inpatient unit of 20-odd patients constitutes a small community, which comprises not only the patients but the staff—psychiatrists, nurses, aides, social worker, psychologist, and activities therapists, with the Attending-in-Charge standing at the head. The purpose of the community is therapy, and when it functions well it becomes a social organism geared to this purpose. This social entity develops into a complex structure, with endless interactions between and within the various subgroups. Understanding the interactions of this small "therapeutic community" and using them for therapeutic ends is a vital part of contemporary residency training. To be sure this community—a well-staffed, highly structured inpatient psychiatric unit, geared to therapy—is hardly the same thing as a ghetto block, wracked by poverty, unemployment, racial dissension, delinquency, drug addiction, and every variety of psychopathology. Nonetheless, many of the essential ingredients of interaction in the larger group can be found, in microcosm, in the small community of a hospital unit. This "little society" may be viewed as a laboratory in which one may observe and learn to deal with group phenomena.† The combination of this experience with the detailed study of the "inner workings" of the individual provides fundamental tools for any one who will later go on to struggle with the problems of the larger community outside the hospital.

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* A word should be said about closed-circuit television as a teaching device. Aware of its potential value, Dr. Kaufman saw to it, a few years ago, that the department acquire television equipment, including facilities for audiovisual tape recording. This marvelous "gadget" has made possible a variety of teaching arrangements of unique value. Patients who manifest classical symptomatology or unusual syndromes can be interviewed before the television cameras with the interviews recorded on tape; these tapes are preserved as a tape library for repeated use in teaching. We have, in addition, used the apparatus to enable residents to watch an experienced clinician in the actual conduct of psychotherapy. The therapy sessions are seen "live," and taped at the same time. The session is then discussed in detail with the teacher-therapist; the tape is available for replaying of any point in the session which becomes the subject of question or discussion. The reverse arrangement has also been used to add a dimension to supervisory teaching: in this case, the preceptor sits before the monitor and watches a resident conducting therapy. The tape can then be studied by resident and preceptor together, to pick up an endless number of nuances and details that are inevitably lost when the resident reports the content of a session from memory and notes. This has proved to be an extraordinarily productive teaching arrangement.

† Group therapy, as such, is conducted in a variety of settings as a specific therapeutic device. All of these varieties of group treatment are part of the residents' training experience.

The outbreak of an acute psychiatric illness very often takes place in a setting of disturbed familial relationships. Frequently the illness of the individual who becomes a patient is only one manifestation of a family crisis. A resident learns this very early as a matter of theory, but the theory becomes reality as he learns to deal not only with the patient who has come into the hospital but with the important members of his family as well. This may be done in various ways. Traditionally the social worker deals with the family and works in close consultation with the resident who is treating the hospitalized patient. But in recent years residents have been encouraged to deal directly with family members also, and in suitable instances to conduct "family therapy," which involves direct therapeutic work with more than one member of the family unit.

In all of these therapeutic endeavors the resident learns to function as part of a "team," even though his is the primary therapeutic responsibility. At various points he will work in collaboration with the nurse, the social worker, the psychologist, the activities therapist, and the school teacher (in the case of younger patients), and he must learn to coordinate his own efforts with the special skills of the other professionals who make up the team.

In addition to the range of psychotherapeutic approaches in use on a modern psychiatric service, the organic forms of treatment are of importance and come into constant play. Our residents are expected to learn the intelligent use of the psychotropic drugs which now occupy an important place in the management of psychiatric illness. They must also know the indications for electro-convulsive therapy ("shock therapy") and the proper procedures employed in its administration.

Along with the preceptors, the unit chiefs (the Attendings-in-Charge of the Inpatient units and the Day and Night Center) stand as primary teachers in the residency program. While the former are concerned with the management of individual patients, the unit chief is responsible for the care of all of the patients on his unit. Twice a week, or more often, each unit chief presides over a conference lasting for an hour and a half and attended by the entire professional staff of his unit. These conferences are the rough equivalent of ward rounds on medicine or surgery, and like ward rounds they perform the closely interwoven functions of patient care and teaching. Patients are discussed both as individuals, and as members of the ward community, and at the same time the functioning of the unit as a social organism comes under continuing scrutiny. The indications for various forms of therapy, and the choice of the optimal therapy for each patient are part of the teaching task of the Unit Chief.*

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* Lest there be any misunderstanding, the fact that psychoanalysis serves as the theoretical basis for both the teaching and the therapeutic functions of our residency program should not lead to the erroneous assumption that our residents conduct psychoanalytic treatment. Our department is not a psychoanalytic training center. Neither the training our residents receive nor the clinical material with which they deal would make it possible to use psychoanalysis as a mode of treatment in the Hospital.

Outpatient Experience

The skills needed for the application of a many-faceted therapeutic approach are not acquired rapidly, and the design of our program gives the residents two full years of work on the inpatient service. In the course of the two years there is a rotation through the Day and Night Center, where they may learn the specialized approaches used in "partial hospitalization." Concurrently with the inpatient experience, work with outpatients begins during the first year. The first outpatient experience is in the Aftercare Clinic, which deals with patients discharged from the inpatient service who need further care on an ambulatory basis. Generally the resident follows his own inpatients when they enter the Aftercare Clinic.

In the second year of training, a very different kind of outpatient experience begins, as the residents take up work with adults who have not previously been hospitalized. The patient population in this clinic is roughly similar to that of an office practice, and consists in the main of people whose functioning has never been so disturbed as to call for inpatient care. In the Outpatient Department the resident must deal alone (except for discussions with supervisors) with patients who live and work in the community; neither he nor his patient has the support of the "therapeutic community." It is here that the skills of individual therapy may be sharpened, and for this purpose the resident continues in the Adult Outpatient Department throughout his second and third years of training.

The Third Year

It has been Dr. Kaufman's conviction that the development of a psychiatrist, if it is to be sound, must begin with a solid foundation in basic psychiatry, and that only after this foundation has been laid down should the trainee go on to what are in actuality applications of psychiatric knowledge and techniques. It is with this in mind that the third year of training has been designed to permit a kind of "branching out."

The Liaison Service, which is described in another chapter of this volume, is closely tied to the name of Dr. M. Ralph Kaufman. It was he who coined the term, and built the Liaison Service into one of the major segments of the department. This division is a concrete expression of his conception of the place of psychoanalysis and psychiatry in relation to the rest of medicine, a conception which is dealt with elsewhere in this volume and need not be repeated here. The Liaison Division has functioned in a way which has aroused the admiration of colleagues from other departments, to say nothing of visitors from other institutions and from governmental granting agencies. Residents in psychiatry become acquainted with the Liaison Service early in their training, when they are asked to respond to urgent consultation requests outside of regular hours. In the third year, however, all residents are assigned to Liaison work for part of every week during a six-month period. In working as the psychiatrist on Medicine, Surgery, or Obstetrics and Gynecology, the resident learns by direct experience how closely interlocked are the physical and emotional components of human illness, and how vital it is to attend to psychological facets of the patient's suffering, even when his primary problem is a somatic one. The idea that there is an emotional component in all illness or that all medicine is truly psychosomatic is one that our residents learn well, and are often the most effective vectors in conveying this concept to their colleagues on the medical and surgical house staffs. At the same time they may develop some expertise in a skill often underdeveloped in psychiatrists, namely, the ability to handle a consultation competently and to communicate an opinion in language that is comprehensible to the non-psychiatrist physician.

An exciting and rapidly developing function of the Liaison Service is the assignment of psychiatrists to the general Emergency Room. In hospitals all over the country Emergency Rooms, standing at the doorstep of the community, have come to play the role of family doctor to the economically disadvantaged. In being assigned to the Emergency Room in his third year, the resident comes into direct contact with the most acute problems of the community. Not only does he render an important service, but he learns to evaluate situations quickly and to make rapid, incisive decisions as to the most effective means of intervention.

The third-year program is at the same time designed to leave time available for elective pursuits. The residents may take additional work in group therapy, in the treatment of adolescents, in community medicine, in forensic psychiatry, or in other areas of individual interest. It is in this last year of the program that a resident who has a bent for investigation may undertake a research project. There are some departments of psychiatry in other institutions in which every resident is required to carry out a piece of research, but we believe that meaningful research is done for the most part by individuals who have an inner motivation for investigative work; "required" research projects tend to become empty and unproductive exercises. In spite of the pressure of ward and clinic duties some residents have managed to carry out excellent studies on clinical problems they have encountered in their first two years; but by and large this is difficult, and the research-oriented individual finds it more feasible to undertake a project in the third year.

Considering the importance of childhood experience in the development of human personality, it is important in the training of a psychiatrist, even if he will never treat children, to have direct clinical experience with the psychiatric problems of childhood. Child development is taught in didactic form in the first two years of the program, but in the third year all the residents are assigned to a parent-child clinic to work directly with young patients, under the supervision of members of the Child Psychiatry Division.

Two other special areas of experience are covered in third year affiliations—neurology and state hospital. Two months are devoted to the former, by assignment of the residents to full-time work on our own Neurology Service. Residents in psychiatry are not expected to become competent neurologists, but they should be able to carry out a satisfactorily informative neurological examination and acquire familiarity with the neurological syndromes which present themselves with some frequency in the everyday clinical practice of the psychiatrist. Another three months are spent at the Manhattan State Hospital in order to offer experience with the chronically psychotic patients who are generally not admitted to our Service.

Didactic Teaching

When our department expanded in 1962 with the move to the new Institute of Psychiatry, the resident staff grew to its present size of 29 (first year, 12; second year, 10; third year, 7), and the dimensions of the teaching program enlarged correspondingly. We devised a rather ambitious didactic program which took up a sizeable number of hours each week. In retrospect, it seems that we were trying to give the resident staff a full post-graduate course in psychiatry through lectures, seminars, and reading courses. It soon became apparent that however good the intent, our zeal was pedagogically misguided. Our residents reported to us that they spent so many hours "in class" as to have difficulty in finding time to see patients and preceptors.* Considering our conviction that supervised clinical work is the central learning experience, it became obvious that the didactic program had to be contracted. We learned also that while for some subjects the course format was effective, for others it was pedagogically unsound.

As a result, the weight of the didactic portion of the program has been progressively reduced. In some cases courses were dropped, in others they were shortened, and in other instances two related courses were amalgamated into one. The result has been that we now have a highly streamlined program, aimed to accomplish two ends—to cover subjects not readily taught in other ways, and to pull together in systematic form concepts which are usually learned piecemeal in the course of clinical teaching. Examples of the first category are a course in the techniques of psychological testing, taught by the Chief Psychologist, and a series of seminars on Psychiatry and the Law, taught jointly by a psychiatrist and a member of the Judiciary. In the second category are three basic seminars: (1) demonstrations by an attending of the technique of psychiatric interviewing, combined with demonstrations of the clinical findings in typical psychiatric disease syndromes; (2) an exposition of the development of human personality from birth onward, taught by a child psychoanalyst, and supplemented by observations of the interactions of mother-child pairs as they attend the Well-Baby Clinic; and (3) a systematic presentation of personality theory, as it is viewed by dynamically-oriented psychiatrists.

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* Long before the recent demands by students for better communication with faculties, we had instituted "feed-back" arrangements in order to know what the residents—as the ultimate "consumers"—felt about their training. The Director of the Department and the Attending-in-Charge of training have maintained an "open-door" policy to permit residents to drop in at any time for discussion of problems or for the airing of complaints. In addition the Attending-in-Charge and his Associate have met with each class of residents during the year for a thorough evaluation of the entire program, including an assessment of the effectiveness of each teacher. The residents have learned that they can be entirely candid in their appraisals, without fear of reprisal, and we have been gratified by the trust they have displayed in openly expressing their opinions of the program as a whole and of their teachers as individuals. Many of the changes made in the program from year to year have grown out of criticisms and suggestions made by residents in these evaluation meetings.

While psychoanalytically-derived theories of personality remain a dominant force, as indicated above, there are views of personality function and therapeutic approach which differ sharply from them. The school of "behavior therapy" has, for example, attracted considerable attention in recent years. At the same time, there are varying viewpoints within the body of dynamic psychiatry, both on theoretical matters and on therapeutic techniques. In order to assure that our residents become acquainted with a variety of viewpoints, we have made a point of inviting, as guest lecturers, colleagues who can present approaches not represented in our own staff. These lectures form an additional portion of the didactic teaching program.

What of the Future?

In the years of Dr. Kaufman's tenure, the Residency Training Program has gone through a process of continuing change. A teaching program can strive for, but never fully achieve, the aims it sets for itself, and in the effort to create a better "fit" between the program and the ideals it embodies, one rethinks, restructures, and redesigns details or whole portions of the program. I cannot recall a year in which the teaching has not been in some way different from the year before. (I believe, indeed, that a program that remains unaltered for any appreciable number of years is likely to be stagnating; stasis in a training program can be as unhealthy as other kinds of stasis.) The brief sketch I have given represents the state to which the teaching had evolved as of 1970; but it should be emphasized that the programmatic changes have taken place within the context of the values and ideals set forth earlier. This kind of gradual evolution will, without question, continue.

But the era of social upheaval in which we are living poses special challenges. Among those essential functions of society which have been the focus of turmoil in recent years, medical care and education are both of leading importance; and this places all forms of medical education, and all varieties of medical educators, somewhere near the eye of the storm.

Here we are concerned with one segment of the education of physicians—the training of residents in psychiatry. My purpose is not to discuss the complex ways in which the social revolution of our time has affected and will continue to affect the field of psychiatry, but only to give examples of the kinds of problems confronting educators in this specialty.

The development of community psychiatry programs has already had an enormous impact on the training of psychiatric residents. The vast mental health needs of all communities, and in particular of the impoverished communities of our cities, have created a pressure for the expansion of mental health care. Some of this expansion entails a wider application of known modalities of therapy; but much of it has meant the invention of new psychiatric techniques applied in novel settings.

In many places the pressure to move into the community has led to an early involvement of residents in community psychiatry programs. In our own department, we have felt it necessary to resist this pressure, for while we share fully the concern for the ills of the community, we have a simultaneous concern for the quality of the training given to the psychiatrists who will in time deal with those ills. The as yet untrained psychiatrist who is thrust into the uncharted waters of community psychiatry may never have the opportunity to acquire the basic tools of his profession; if this were done on a large scale, the result could only be a deterioration in the quality of training and in the ultimate level of psychiatric competence.

Yet the need to learn how to deal effectively with mental health problems on a broad scale cannot be denied and it is here that the challenge lies: how to include in a training program the experience of dealing with community problems without at the same time sacrificing the essentials of good training, for the mere "delivery" of well-intentioned psychiatrists to the community is not enough.

As America has come to the belated recognition that it has a grossly deficient system of medical care delivery (a "non-system" it has been aptly called), medical school curricula and hospital training have begun to change radically. Within the past year, the effort to shorten the total span of years needed to train medical specialists has led to moves that will before long do away with the year of training traditionally called the internship. The Specialty Boards in Psychiatry, among others, have eliminated the year of internship as a requirement for Board Certification. Our Department, along with many others, views this as a deplorable development for psychiatry, and for the present has continued to require an internship as a pre-requisite for residency training. But from all indications this will only be a temporary holding action; in time it is likely that all departments of psychiatry will, whatever their objections, have no choice but to accept trainees coming directly from medical school.

When that time comes, training programs in psychiatry will be confronted with a serious problem. The year of internship is, for the psychiatrist, the only opportunity in his learning years to deal directly with physical illness, and to carry life and death responsibilities. It is also a year in which the young physician begins to develop a clear sense of his identity as a physician. For the future psychiatrist (more than for other specialists), these essential growth experiences will be missed, since the clinical problems in psychiatry are of a different nature from those in medicine or surgery. A generation of psychiatrists who have never worked on non-psychiatric hospital wards will, we suspect, not have the close tie with medicine which we feel is important for both medicine and psychiatry, and which we have emphasized so much in both teaching and practice.

In time, medical school curricula may offer something equivalent to the internship, as some schools are already endeavoring to do; but in the meanwhile, the excision of this important segment of training presents a problem to those responsible for the training of psychiatrists. That which has been excised will in some way have to be replaced during the three residency years—three years that are already bulging out of their calendars. We are faced with the necessity of a considerable restructuring of the training program in order to meet this new situation.

I have cited these examples of problems we face not in order to demonstrate how dreadful things are, but for a very different reason: to indicate the spirit in which they will be confronted. The Mount Sinai training program has been attentively thought out, carefully structured, and solidly organized. It is a well-knit, smoothly functioning organism, whose teaching staff is large in size, high in morale and undiminished in its enthusiasm. Our feeling is that whatever difficulties we may encounter, we are as well equipped to meet them as a teaching staff could possibly be.

I can think of no greater tribute to Dr. Kaufman as he ends his tenure than to say that this is the state of healthy vigor in which he will leave the training program that he inspired.

Evolving Social Services in Psychiatry

DORIS SIEGEL, M.S. AND HELEN REHR, D.S.W.

The history of medical and psychiatric social work in the United States is linked closely to the historical developments in medicine and in psychiatry. Social work turned to the leaders in health care for its origins in evolving services to individuals and in creating programs of social reform. The professions of medicine and of social work have a long history of mutual concerns and relationships, and project a future of continuing inter-relationship in the delivery of social-health services.

The history of medical and nursing care in this country during the eighteenth and nineteenth centuries shows the development of a proprietary type of medical institution, indigenous to the New World. The unprecedentedly rapid growth of population over enormous expanses of territory created a demand for doctors long before facilities for training existed. The pioneering condition of the country fostered the manufacture of thousands of physicians by commercial correspondence schools. These prospective doctors, who developed little knowledge or skill from these courses, often paid for their apprenticeship training in hospitals set up by municipalities, religious organizations, or philanthropic groups, to serve the poor (1). Concurrently, the women who pioneered in medicine were the forerunners of the social service movement in health care. In New York City Dr. Elizabeth Blackwell, who has been credited with opening medical education to women, was also responsible for social services to the sick poor. In 1853 she secured the establishment of a dispensary to serve the poor sick women and children of the East Side as a training center for women doctors. In 1866 Dr. Blackwell created the position of "sanitary visitor" whose responsibility was to visit the homes of discharged ward patients and selected outpatients (2). The report on the functions of that early "visitor" one hundred years ago is remarkable for its pertinence to today's issues in social work. "Entering into conversations with the mother or father, she ascertained the various facts relative to the physical condition of the family. The visitor brought up subjects of ventilation, cleanliness, warmth, food, and clothing, making practical suggestions as they seem to be needed in each case. She sometimes taught [cooking and economical choosing of food]. If nuisances [were] found, they were reported to the proper authorities and speedily removed. Employment was often found for those who needed it, for though the work is educational, rather than benevolent, pressing physical wants must be supplied before any improvement can be attempted" (3).

Home visiting was continued by the doctors at the forerunner of the New York Infirmary for Women and Children, as well as the precursor of the New England Hospital for Women and Children in Boston. It was also Dr. Blackwell's intention to help medical students understand slum conditions and social health problems related to sweatshops and child labor. This early evidence of medicine's concern with the social components of illness moved from doctors to nurses, and finally lead to the development of social workers.

A similar movement was underway in the field of psychiatry. In the 1870's the National Conference of Charities and Corrections voiced concern with the social issues related to mental disorders. Those social workers and psychiatrists were familiar with the problems presented by patients, formerly hospitalized in asylums, returned to unprepared and unreceptive homes and communities and without any available economic opportunities. These conditions frequently necessitated their remaining in the asylum or transferring to a poorhouse. When Dr. Adolph Meyer took over the then Pathological Institute connected with Manhattan State Hospital, he enlisted Mrs. Meyer in visiting his patients and their families to seek social and economic data which he believed affected living conditions. With the support of The American Neurological Institute, and of prominent psychiatrists and social workers, he secured the sponsorship of the Aftercare Movement under the aegis of the State Charities Aid Association as early as 1892. In 1906 the Manhattan Aftercare Clinic Committee started with a social worker "to provide adequate financial, medical, and moral assistance to patients discharged from mental hospitals in order to aid in their adjustment to the outer world and to check relapses due to social handicaps." (4).

Before the last decade of the nineteenth century, the Johns Hopkins Medical School, created in Baltimore, offered a medical education modeled after the German university style of the master-professor "impregnated with scientific ideals" (5). The new school of thought represented by Sir William Osler taught medical students to look beyond the purely physical for diagnostic and therapeutic media.

"It was for this reason, in 1902," recalled Dr. Charles P. Emerson, a student of Osler's, "that many of the medical students of the Johns Hopkins University organized themselves in classes to study the patient in his home and so to understand more clearly the problem of diagnosis and therapy involved. Fortunately we had no difficulties with the Baltimore Charity Organization Society (those connected directly or indirectly with the Johns Hopkins University sometimes formed almost a majority of those present at the directors' meetings). Since we, as medical workers, were interested in many of the very same families which they as charity workers had for years been helping, we used their officers, their trained workers, and other personnel, and did not need to start a *rival* organization" (6).

These ideas of orienting medical students to the social factors in illness were in keeping with a new philosophy prevalent at the turn of the century. Belief was shifting from the rigid conviction that man's lot was an unchanging one to a blossoming emphasis, led by the Reform Darwinists, on man's ability to modify his environment to afford himself new opportunities. Social reform and social justice were the keywords of the times. In the medical context the social environment was seen as causative of illness, and important in diagnosis and in therapy. The significance of infection, communicability, the environment, and the community had taken hold in the medical elite among such men as Drs. Cabot, Emerson, Chapen, and Meyer. They were strongly motivated toward including in medical knowledge a social dimension lodged in the environment. Dr. Cabot identified tuberculosis as most responsible for "socializing" medical diagnosis and treatment, since its treatment required modifying the environment. Tuberculosis was also credited with pointing out the significance of the individual human being as a necessary factor in his own treatment, thus shifting the doctor's view of his patient as an inert body to which treatment was ministered. At Johns Hopkins and at Harvard such ideas as prevention of illnesses, social reform to better the social environment, and a beginning awareness of the individual in the setting of a family were introduced into medical education (7). Another concern also arose—how to make certain that only the "worthy poor" benefited from the largesse of the rich and from the charity of the medical practitioner.

With these social issues on the horizon, a marriage between medicine and social work came into being at the turn of the century. This mutual interdependence in education and in service led to a concept of medical-social orientation. A specific place for social work in medical care programs was carved out in this period of high motivation and commitment. The first formal development was Dr. Cabot's creation of social services at the Massachusetts General Hospital. The credo of these services was to assist patients in whatever way possible to follow medical recommendations and to keep the physician informed about his patients so that he could adjust his recommendations accordingly (8). The initial roles of these social workers were patient-family centered, socially-environmentally oriented, and institution- or physician-based. For a half century, these early objectives remained the basic tenets of social work in health care settings, while the profession grew in finding its methods to achieve these goals. The Mount Sinai Hospital soon adopted these goals.

From its inception The Mount Sinai Hospital has been in the forefront of medical and psychiatric advancement and has been a leader in social work programs as well. The Social Welfare Department was established by the Hospital's Board of Trustees in 1906, with the urging of Dr. S. S. Goldwater. That program was initiated to aid patients discharged from the wards with their medical, convalescent, and employment needs. It soon took on the concern of tuberculosis prevention as part of a city-wide program. The nurses-turned-social workers evolved a social service program in which they used a variety of data-collecting means, made home visits, gave advice, cooperated with other social agencies, instructed mothers in the care of their children, located financial and clothing assistance, and found employment for patients and recreational outlets for children (9). The hospital, through its physicians, established a Children's Health Class for preschool children in 1919 to deal with the "preservation of health" (10). This was a forerunner of The Child Guidance Movement of the twenties. With the growth in Psychiatry following World War I, the hospital created a Mental Health Clinic in 1920, thereby separating the mental health concept of care from a neurological emphasis. A social worker was added to the program in 1922 (11).

During the next quarter century, the emphasis in the health care field took two pathways: one, dealing with public health, social-environmental and sociological problems, and the second with diagnostic and therapeutic advances. It was in this latter direction that social work sought to place its major thrust, concentrating its skills in developing the social casework method as a social treatment modality for dealing with individual needs. The Mary Richmond concept of a systematic approach to social diagnosis was compatible with methods employed by scientific medicine. Awareness grew that an individual's qualities combined with his circumstances were determinants in how a person would conduct himself. Emphasis on personality theory led to understanding the inner forces which mold behavior and determine an individual's goals and achievements. The psychological significance of the therapeutic relationship was learned from Freudian dynamic psychiatry. The largest part of social work's endeavors was concentrated on the clinical approach to social problems related to medical or psychiatric illness.

Social work's proximity to the advancements in psychiatric programs for individuals and their family members at Mount Sinai Hospital permitted it to enhance its social treatment methods, and at the same time to contribute to broadening the psychiatrists' view of man's social environment and the effect of social stress upon personality.

1970: Looking Back at Twenty-Five Years of Social Services at The Mount Sinai Hospital

In the twenty-five years following World War II, psychiatric services have come into greater recognition and acceptance by the public. At Mount Sinai Hospital psychiatry has contributed more in service to patients regardless of location in the institution and to collaborative interrelationships during this period than at any other time in its existence at the hospital. Its influence on social-health care services to individuals has been both direct and indirect.

The basic philosophy of the Social Service Department, and of course, that of Psychiatry, is directed toward positive health, defined in the World Health Organization sense not only as the absence of disease but also as the achievement of physical, social, and emotional well being. The Department is committed to the consideration of the patient as a person. Its primary focus has been the many social and emotional factors which contribute to or accompany illness and interfere with the patient and family in achieving optimum health status. Social work in the general hospital has recognized the power of social and personal circumstances to influence health status and to affect the capacity of patients and families to obtain and use health services. It recognizes the need for a family-centered approach to health and medical care and it views such an approach as applying to all phases of care from detection through diagnosis, treatment, and rehabilitation. It moves beyond concern for the individual and individuals in small groups to a recognition of the importance of societal provisions for the promotion and maintenance of health and the prevention and treatment of disease, to an understanding of the value of community services and social health planning, and to the exploitation of all available methods of intervention. Social work, in pursuing the philosophy outlined, carries forward mental health concepts in its work not only in psychiatry but in all the services of the medical center: for example, medical, surgical, obstetrical and pediatric programs for inpatients and outpatients. It is able to do this through training in such topics as personality theory, family organization, social sciences, social stress, social change, and systems of intervention, as well as the understanding of the significance of cultural differences and the impact of poverty.

The Social Service Department serves many of the systems in the medical center. It serves patients and families directly by utilizing the methods of social casework, joint and family interviewing, and group programs. It serves its physician and nursing colleagues by consultation on behalf of patients. The department plays a direct role in program development and in modification of the overall Medical Center's community of services. It works with lay leaders and with members of the local community. It has an educational role not only in the development of its own students, but also with students in the other health care professions who serve in the institution.

Social workers carry the role of advocate in speaking for the patient in the many service systems which the patient encounters both within and outside the hospital. The social worker may serve as a negotiator in behalf of the patient as well, and often as a coordinator of the many facets of his care.

In order to carry out its philosophy, and in line with the functions and roles identified, the Social Service Department at Mount Sinai Hospital has developed an organized system of programs and services. The system functions through one Social Service Department—a unified department. In this context all staff who provide social services to patients, and related services and consultation to others, regardless of the source of these requests, are members of one department, responsible to it and nurtured by it for professional direction. The advantage of this unified system is that all social services in the institution are benefited by the accumulated experience, thinking, and ideas represented by the department as a whole. Each unit of the service, whether as an individual worker or as the group of social workers assigned to Child, Adolescent, or Adult Psychiatry, or Medical, Surgical, Pediatric or Obstetrical Services for inpatient or ambulatory patients, offers the others enrichment of ideas, practices, and programs through a continuing exchange. The unified department enhances specific programs through its collective strength, experience, wisdom, and resources. Thus, it is more than the sum of its parts. This unified approach to social service programs in a general hospital serving both medically and psychiatrically ill patients escapes the hazards of isolation, not infrequently observed in the autonomous programs found in some medical institutions. It is our belief that through the opportunities derived from its overall experience the unified social service department has made an important contribution to the socialization of the total hospital. In addition, the social work skills and modalities of care can become readily available to patients in any section of the institution where they may be applied (12). The Social Service Department's assistance to patients in the general hospital and to their families, is illustrated in the Institute of Psychiatry, where the social workers have contributed to the programs and to the psychiatric staff working in them. At the same time, through its staff in other departments of the hospital Social Service has made effective use of its learning from Psychiatry.

Psychiatry and the Social Services at The Mount Sinai Hospital

The twenty-five years which have just passed represent peak developments in psychiatry and social work which are attributable to the man who has directed the Department of Psychiatry over that period. The philosophy which characterizes best the psychiatrist and the man in Dr. M. Ralph Kaufman is a belief in the individual and in his worth as self, in his family, and in society. The basic aim in psychotherapy at Mount Sinai Hospital has been to enhance the individual's coping ability and social functioning (13). The primary focus of social work in this setting has been on the individual and his family in relation to their social-environment and on the inner and outer resources available to them—a philosophy compatible with Psychiatry's. During these years the social work development and emphasis have been not with the social problems or the social issues of the day, but rather with the principle of individualization. This has been effected through a key method in the social work armamentarium—social casework. Its purpose is to restore and improve the social functioning of an individual and his family by dealing with the problems in their "person-to-person or person-to-circumstance encounters" (14). The current trend in social casework has shifted from "concentration upon the person as self to concentration upon the self in continuous interaction with other selves within a dynamic social situation" (15).

The progressive enrichment of the profession through the development of social casework and related methods serving the individual and his family has been due to many factors. These include, during the years and up to the present: its early emphasis on guiding the "worthy poor"; its work in social reform; its development of a social diagnostic approach; its articulation of a common base of practice among social caseworkers regardless of where they practiced; its introduction of Freudian concepts to understand the inner forces that mold human behavior and the significance of therapeutic relationships; its focus on ego psychology dealing with man's coping and adaptive means in relation to his social environment; its perception of the effects of social stress from such critical events as the Depression, and the Wars; and its introduction of social science ideas such as social roles, cultural identification, class differences, social instability, social change and learning theory (16). As this knowledge has developed, the profession of social work has used it to enhance its practice in many settings. At The Mount Sinai Hospital, the Psychiatric Division has contributed to the inclusion of these concepts into the social services by its encouragement and support. Yet at the same time it has sought to strengthen the different professional contributions to the team effort on behalf of patients and their families. The leadership in the Psychiatric Division has fostered the belief of the integral contribution of professional experts with a minimum of the role confusion that has sometimes been noted elsewhere. "In many multidisciplinary settings," according to one observer, "the primary function of each profession in a clinical team has been subordinated or even defaced as social workers, psychologists, and psychiatrists have become psychotherapists operating with negligible difference from one another, and the psychiatrist has become more consultant, supervisor, and teacher than practitioner of his specialty" (17). This is not so at Mount Sinai, where social work, psychology and psychiatry, as well as nursing, occupational and recreational therapy, and other professions have enriched each other by contributing their own individual and specific expertise to a more comprehensive approach. For social work, the experience has meant the development of social casework from an early focus on problems to a consideration of the complexity of person or persons—"a union of psychic and social" (18)—with neither replacing the other. Central to casework is the notion of "the person-in-his-situation" (19) which consists of the person, his situation, and the interaction between the two. As a psychosocial treatment method, casework "recognizes both internal psychological and external social causes of dysfunctioning, and endeavors to enable the individual to meet his needs more fully and to function more adequately in his social relationships" (20).

The casework concepts and related methods have been implemented in many ways in the social work program at Mount Sinai's Institute of Psychiatry, where the worker is responsible for making a social diagnosis, setting goals with the family and using various social work treatment modalities, including the use of himself in an interpersonal relationship as well as of his knowledge of both hospital and community resources. It is clear that psychiatric illness has a strong impact on the individual's social relationships, employment status, recreational outlets, and family relationships, often necessitating changes in roles and responsibilities. The ability of the patient to cope with his daily life situation may be enhanced or blocked by attitudes and actions of his family, which may influence his motivation toward health and rehabilitation. Accordingly, work with the family has been an essential component of the program of this psychiatric service.

A family-centered orientation has always been part of the total program of the Social Service Department at Mount Sinai. Various members of a family may be seen in relation to the patient hospitalized on a psychiatric unit. Social workers in the Psychiatric Division have used the valuable method of the joint interview to see both parents together on behalf of a child or in relation to their marital compatibility. In the past several years joint interviews have become a major modality of social service functioning. These have expanded from the triad of social worker and two key family members to include the psychiatrist, either resident or attending, and a psychiatric nurse, when deemed helpful. This method has proved of real value in helping family members to see their role in relation to a patient's illness and also in strengthening their understanding and ability to provide support as plans are made for his return home. Although slow, there has been a decided increase in the development of the family treatment modality with a multidiscipline emphasis that is no longer limited to specific members of the family, but includes the total family group.

Direct work with the family concerned about a member who is a patient in the psychiatric service of a general hospital calls for considerable social work skill. Because a rapid treatment approach is the rule (21), limited by and large to a 90-day maximum inpatient stay, careful screening is necessary and admission must be restricted to those who it is believed can benefit from the program. This rapid treatment approach calls both for diagnostic acumen and for an astute ability to make social assessments of the "person-in-his-situation."

In addition to the major utilization of the one-to-one method between family member and social worker, and the extended use of the joint-family social treatment method, social work has expanded its use of group services over the last several years. Beginning first with group counseling, the Department has moved also into work with self-help groups and spontaneously formed groups. Our experience has indicated the value of this approach in helping patients and families reach therapeutic goals.

Staff members also have served as leaders of inpatient groups, particularly in helping them adjust to the realities they will be facing after discharge. For example, a group of patients in their late teens and early twenties who had been hospitalized in psychiatry met to consider what might be involved for them in facing the job market. They discussed attitudes about explaining the period away from any work, anticipated rejection, as well as their image and assessment of their own worth. This effort to meet a day-to-day-living problem proved to be extremely helpful.

The social work staff has also been particularly effective in meeting with groups of older patients and offering both practical help and support for their many problems which are heavily involved with social realities as well as with emotional reactions to these same realities. Group members have gathered strength from each other's coping ability. In addition, social work has been involved in a co-leadership role in which both psychiatrist and social worker take therapeutic roles defined by the group needs.

Skills in social work methods are evidenced in all sections of the medical institution. They are particularly enhanced by the services of Liaison Psychiatry which are available to any patients being treated in the Medical, Surgical, Pediatric or Obstetrical-Gynecological Divisions, and any subspecialty within these areas. Social work and Liaison Psychiatry have had a joint collaborative relationship in regard to patient care, teaching, and consultation from the beginning of this program. In some instances, through its assignments to the different service areas, social work has paved the way for psychiatric intervention. At the same time it has benefited from psychiatric consultation on behalf of patients it is serving. The value of this interrelationship has extended to both the inpatient and outpatient areas.

The emergence of the concept of the therapeutic community has been a development of considerable interest to Social Service. As demonstrated in a number of areas of the Mount Sinai Psychiatric Program, it uses all the resources of the hospital and its personnel toward involving patients in their own care and striving toward health. Psychiatry's utilization of various group and individual efforts helps each to look at professional differences, to give voice to them and at the same time to permit a team effort to occur. The philosophy of the therapeutic milieu is in keeping with the philosophy promulgated by the Mount Sinai leadership in psychiatry. The atmosphere of the Institute is intended to be as close as possible to what the patient may encounter outside the hospital. While psychiatry's "open door" policy has permitted occasional "elopements" (leaving against advice), it has symbolically diminished the discrepancy between "inside" and "outside" and has thereby fostered the individual patient's belief that he can return to adequate social functioning in his own environment. Within the hospital itself a milieu is set up which hopefully creates a bridge to the more rigorous demands of community life. Through encouragement to concern himself with his own care the patient may shift from a passive to an active role, and even assume certain responsibilities. In a large sense this method relies on the principle that one can help people help themselves by their helping others. Social distance between staff and patient is lessened, so that more direct communication is possible.

In this kind of climate each component of the staff has an opportunity to make a special contribution. This is certainly true in relation to Social Service. The efforts within the hospital in this development have been significant and satisfying. It is also clear that like other components the contribution of Social Service must be made in partnership with other disciplines; indeed collaboration is essential in order to permit each discipline to use the findings and understandings of others in making its own contribution.

Through its skills in providing consultation, social work at The Mount Sinai Hospital has offered assistance to professional and subprofessional persons outside the health care system in relation to some social and emotional factors affecting the psychiatric patient. For example, there are many telephone inquiries addressed to workers in relation to patients or clients, many of which come from other agencies within the community which may not have available to them the expert knowledge and skill often possessed by the staff within the department. Discussion of the criteria for and the mechanics of admission to a psychiatric unit, to the Day and Night Treatment Center or to the Outpatient Department, for instance, may lead to recommendations for consideration of one of these alternatives. On the other hand, such a consultation may suggest other solutions as more appropriate. Whether or not the recommendations are accepted, they usually transmit some added dimension in regard to an understanding of the behavior and personality of the individual under consideration together with possible avenues for help.

At times, individuals on the hospital psychiatric staff have utilized members of the Social Service Department for consultation on various resources and services available in the community that might be called upon for private patients or families of their patients. The schools have been another source of request for consultation. Faced as they are with many acting-out children, they constantly turn for assistance and for some answers to what appear to be insoluble problems. Nevertheless, it has been possible at times to offer constructive and positive help through consultation. Together with a psychiatrist, a member of the Social Service Department has worked closely with school and guidance personnel in helping teachers examine and understand their own attitudes toward children who pose problems in studying and learning. The team has offered increased and deepened understanding of the intrapersonal and social problems faced by the youngsters and their families. In a special program carried by the Department of Psychiatry in a local school, a very significant contribution was made through a joint team working with school personnel. A most meaningful consequence of the involvement of social work in this consultation process was the benefit it brought not only to the children immediately concerned but, we believe, to other classes where the same teaching personnel participated.

Reference has been made to the many programs of the Department of Psychiatry within the general hospital and in its nearby community. Social work has been a participating member of the planning group for program development within the Department of Psychiatry. Workers in Psychiatry have also participated in programming for the hospital at large. Social workers in all programs have brought together their expert knowledge of the social problems and social needs of patients. They have let it be known where hospital policies and procedures have had a negative effect on the care of patients, families and the community. The Social Service Department has highlighted the problems in the Outpatient Department's service and has pushed for a more comprehensive, coordinated program of care for patients. Using day-by-day experiences, incidents have been used to point out procedures which interfere with securing good care and to identify policies that even put obstacles in the way of getting any care whatever. Social Service has also attempted to focus beyond the individual patient to larger clinic populations by pressing for action for given changes. One such effort is the department's creation of a Patient Service Representative Program—a kind of ombudsman and "trouble shooting" service. People in the local community as well as in the hospital have used this service to trace instances wherein individual patients have been blocked by bureaucratic obstacles within the hospital. It is the purpose of the Patient Service Representative Program to effect changes in hospital policy and procedures by a feedback system which highlights recurrent problems with the delivery of care to patient, so that such conditions may be altered.

The emphasis in recent years on better services to people in the ghetto communities has had its impact on both the Psychiatric and Social Service Departments of The Mount Sinai Hospital. Psychiatry has developed a service for the segment of the population in the nearby area which utilizes the emergency room of the hospital. The immediate availability of psychiatry for patients suffering from an acute and transitory episode of mental illness has eliminated the so-called "revolving door" procedure of so many emergency rooms. Patients no longer have to express their complaints in the language of the specialists' system in order to reach the appropriate and needed service. The prompt availability of psychiatry is in response to a patient's symptoms rather than to his skill in asking for the particular expert necessary.

Social Service has expanded its services to persons in the East Harlem area, by creating a program of social-health "advocates." Social-health advocates are individuals who live in the local community and know its constituents. They serve as a bridge between the hospital and community, giving special attention to interpreting hospital services and to enabling community residents to use services more fully. One social-health advocate is assigned to the Community Child Psychiatry Clinic and has proven a most effective addition to the team. At Mount Sinai, the advocates have come from work in many of the service systems in the East Harlem area. They know the schools, the Welfare Department, settlement houses, housing agencies and other programs, and the deficiencies of the program in their own community. They are advocates for their fellow residents for services they should receive, and they serve to enlighten the hospital staff concerning the difficulties in obtaining care in the area.

A Look Ahead

We have related this paper to the basic tenet inherent in the psychiatric service programs at Mount Sinai Hospital under the leadership of Dr. M. Ralph Kaufman. His credo of "individual worth" and individualization of the human being to foster his well-being has been the underpinning of all inpatient and ambulatory care programs in the Institute of Psychiatry and in the general hospital. In these troubled times those services designed for the individual in need have fallen under attack. Social work, with its emphasis on the methods of social casework and group services as helping processes to persons and families in need, has been singled out, along with psychiatry, for its failure to deal with social problems which affect society and large sectors of the population. These critics have felt that the psychiatric and social work lenses have been too constricted and the scope too confining. In one sense they are right. We need to view and include the social basis of mental health problems (22), and the social treatment of problems in the environment must be an intrinsic part of the planning of both these professions. We must operate in a larger arena, concerning ourselves with sectors of the population as they are affected by their socioeconomic status, and with such broad social issues as the effects on the population of unending wars, of continuing racism, and of the countless varieties of pollution. Mental health is as much a product of the human social and physical environment as it is of the individual's inner drives and motivating forces and as such its attainment transcends the potential of the disciplines of psychiatry and social work. However, these professions can play important roles in the problem-solving and decision-making required to correct the ailments of our society. With professional commitment to work in these areas, there must also be commitment to involve those most affected by societal ills. Representatives of the beneficiaries of social changes will need to be active participants in the planning for those changes. The layman no less than the expert must be willing to do his part in pursuing practical and imaginative approaches to mental health. While the ways are not clear, the data are before us. The impact of social diseases can be systematically documented and proposals to deal with them can be offered.

Yet despite the urgent need to abolish poverty and to provide adequate food and shelter, and the opportunity for a decent way of life, the road to mental health cannot be traversed. We can learn from the social scientists on how to quantify the impact of the data and from the planners will come help with the experiments. Such measures can never eliminate the need for clinical care for the individual, or for personal or family treatment services. The person-in-his-situation constitutes the unvarying uniqueness of the individual in any society. While the quantification of data by the social scientists may suggest the sociological problem and the trend, it does not account for the individual and his unique place in his group and in society. The individual with emotional problems will always require a system of care from knowledgeable experts. We believe the following aptly puts the situation at this time: "Neither psychological treatment that holds the environment constant and directs its attention primarily to individual adaptation, nor social treatment that holds the individual constant and focuses on changing the environment can alone be an effective agent of change" (23). If we are to be of service, both approaches must be integrated. The person, the problem, the task, and the program are more important than how the turf is carved up by the professional experts. Expert knowledge and skills are required for enhancement of the environment in which we all live, and for the individual in need.

The skills known to therapists through observation of the individual in his daily life patterns and by hearing what he tells us about it are the skills enhanced during a quarter of a century of practice with a patient-family care system at this institution. Those skills, the knowledge of human problems and of individual coping ability under social and psychological stress can contribute to today's (not tomorrow's) planning to bring about essential social changes. The individual in need cannot be forgotten and a knowledge of the means of developing his "self-worth" continues to be a necessary dimension in the different systems of human services.

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Psychological Medicine in a Postgraduate Program

HANS J. KLEINSCHMIDT, M.D.

The need for "a second education" or re-education of the physician to enable him to deal with the emotional problems of his patients was already recognized by Feuchtersleben in 1845 (1). More than fifty years later, Theodor Ziehen, Chief of the Department of Psychiatry at the Charité in Berlin, arguing the validity of psychotherapy, commented: "Even if one disregards all previous arguments, there is one main justification for psychotherapy: every case of sickness involves psychotherapy. One can mend shoes or graft plants without psychotherapy, but one cannot heal the feeling and thinking organism which is man without it. Indeed, every doctor practices some kind of psychotherapy, to be sure, mostly instinctively. Psychotherapeutically we win and keep the allegiance of the patient. Finally, as concerns psychic illnesses and their much-mentioned psychic overlay of pure physical symptoms, psychotherapeutic methods far excel all others in effectiveness and significance. Psychology and psychotherapy must stop being the stepchildren of practical medicine" (2).

This quote well illustrates the prevailing attitude among physicians during the nineteenth century toward the establishing of a discipline of psychological medicine. Feuchtersleben, Ziehen, and other pioneers were faced with the dilemma of first demonstrating the validity of psychotherapy itself. But even Freud's revolutionary contribution could not insure a ready consideration or acknowledgment of the role of psychological factors in physical illness.

In America, the formal beginning of the dialogue between the psychiatric and medical communities is generally considered to have been the Minnesota Project in 1946 (3). This project was set up as an experimental program to study the possibilities of educating physicians in general medical practice in the fundamentals of psychiatry. Although the purpose of the two-week program was to enable the practitioner to become more sensitive to the emotional problems of their patients, the seemingly limited goal involved in most instances a reconciliation of the mechanistic etiology in which the physician had been trained with a nonquantitative and an abstract method of thinking.

But already in 1933, Dr. Kaufman had initiated an investigative and educational program of psychological medicine at the Beth Israel Hospital in Boston. In an article reporting on this early teaching experience, entitled "Present Methods of Teaching," written in collaboration with Felix Deutsch and Herrman Blumgart, Dr. Kaufman remarked: "The intimate relationship between psychological factors and bodily function has always been recognized in medicine, but the task of conveying the importance of this relationship to medical students has depended more on the individual teacher's interest than on any considered program" (4).

In 1962, Sheeley found that demands for postgraduate psychiatric training had resulted in a sharp increase in the number of courses and seminars for nonpsychiatrist physicians (5). In fact, in 1970, in the New York area alone, out of a total of 362 postgraduate courses, 128 were in the field of psychiatry. On first examination of these statistics one might conclude that no longer is there a problem in the dissemination of psychiatric knowledge within the medical community. But it is general knowledge that even with the increased demand for postgraduate courses in psychiatry, only eight to ten percent of the total medical community were actively interested in joining such programs. Just as the history of psychological medicine demonstrates a fundamental dispute over methods of teaching which involves and underscores two differing philosophies of method and medicine, an examination of the 128 postgraduate courses in psychiatry during the academic year 1969/70 reveals the underlying problem: the lack of a unifying theory which would provide an acceptable basis for psychological medicine.

The lack of response in the medical profession has been rationalized for some time by the psychiatric community in terms of purely psychological resistances. These factors may be partially or wholly valid, but it has been a mistake to overlook the enormous cognitive issues involved in setting up an interdisciplinary program in psychological medicine. These problems are part and parcel of the Leavis-Snow "Two Cultures" controversy between science and philosophy (6). The essential problem in both instances is the search for a methodology which in some way encompasses, at least partially, two different sets of phenomena.

At Mount Sinai's Institute of Psychiatry, the essential problem of reconciling these two very different disciplines has not been totally solved; however, under the aegis of Dr. Kaufman considerable efforts have been made to isolate and deal with problems in methodology in the new field of psychological medicine.

Staff members at Mount Sinai Hospital have often heard Dr. Kaufman say that psychiatry is an indivisible part of medicine. If the medical practitioner is to be enabled to incorporate psychological principles in his day to day practice, then he must be educated in these principles, but within a medical framework. Although this point might seem obvious to some readers or obscure to others, it is around this very issue that the difficulties and controversies in teaching psychotherapeutic medicine have revolved.

In the early fifties, several attempts were made at The Mount Sinai Hospital to provide programs in psychiatry for the nonpsychiatrist physician. These early courses consisted of lectures, alternating with discussions of case histories and of clinical problems which the student-physicians encountered in their practices. The physicians met once a week for half a day over a period of twenty weeks. These early courses were not very successful, since both the teaching staff and the participating physicians came to realize that a significant change in the practice of the physician had not taken place. It was soon discovered that the absence of intensive clinical experience and the presentation of psychiatric abstractions rather than the presentation of psychological *medical* concepts resulted in a very limited success.

In 1959, a postgraduate course in psychiatry for medical practitioners and specialists was set up at The Mount Sinai Hospital. The course was structured around clinical work in supervised sessions with suitable patients from different departments of the general hospital and had as one of its primary goals the live demonstration in case after case of "the fundamental tenet that psychopathology can, and often does, coexist with organic findings" (7). But equally important was the emphasis on emotional reactions in patients about to be hospitalized for surgery or a diagnostic work-up or any physical illness. Had the patient about to be discharged after recovery from a myocardial infarct been given an opportunity to talk about his fears? Had he been asked about insomnia and depression or merely been told what pill to take in case of anginal pain? Should the patient who is worried about "possible after-effects" of his prostatectomy be encouraged to talk about his anticipatory anxiety concerning his postoperative sex life?

The course extends over a period of nine months. It is given by a teaching staff consisting of three psychiatrists, a psychologist, a social worker, and a supervisor of the technical staff. Originally, it took place two mornings each week, on Wednesday and Saturday from 9:00 A.M. to 1:00 P.M. Through screening interviews, a minimum of six, but not more than eight physicians were selected out of the total group of applicants (8). But in the twelve-year period in which this course and its follow-up seminar has been offered, there has been a significant increase in the number of students. Last year, twenty physicians took part in the program. This was accomplished by dividing the course into two separate sessions. In addition, there were eleven physicians in the follow-up seminar, who had previously taken the basic course. Of the twenty doctors enrolled in the basic course in the academic year 1969/70, fifteen were general practitioners engaged in private practice, one a medical officer on active duty in the U.S. Army, two were internists, one a cardiologist, and one an oral surgeon. Five physicians, who had previously taken the course and were unable to attend the evening sessions of the follow-up seminar, participated as externs attending the conferences and seminars. Two of these were general practitioners, one a plastic surgeon, one a pediatrician, and one a gynecologist.

Having restructured the program, we now are able to train more than twice the number of physicians each year. This was done in order to meet the growing needs of the community. We now have two groups of physicians with ten in each group—one group meeting Wednesday and the other meeting Saturday for four hours. Each of the twenty physicians is given the opportunity to work with clinic patients in a supervised setting. During the nine months of the program, the twenty physicians are assigned from three to six patients each for brief psychotherapy with clearly defined limited goals. In addition, formal lectures and seminars are structured around the experiential training. Throughout, the emphasis is placed on a clinical approach where the patient is the central focus. The teaching, therefore, concentrates on specific problems that arise in the course of each doctor's work with patients he is actually treating.

Like the medical student and the intern, the physician who attends a postgraduate course expects "structure" and hard and fast rules which he can apply in his practice. He is justifiably critical of vague generalities. Particularly irritating to him are references and admonitions to the effect that he ought to take more time to "just listen" to his patients in order to understand their problems in coping with life. It should be obvious that he comes to us precisely because he does not know how to evaluate and sort out what he is listening to. How often have we heard from out student-physicians that they felt on alien ground, that they had to first unlearn deeply ingrained routines, behavior patterns, and trends of thought before they were able to accept the unfamiliar orientation inherent in a psychological approach to their patients. Used to the active role of healer who "does something" with the aim of providing immediate relief from suffering and removal of symptoms, the invitation to first make his own emotional reactions of fear, impatience, annoyance, and outright anger at his patients available to conscious inspection and analysis and then to look for similar emotions in his patient's story of psychic distress, must be unsettling to the physician who has trained himself to adopt a "professional" attitude and bedside manner by relying on defensive operations which helped him to "control" such emotional reactions. It is true that "much of the learning in the early sessions hinges on making preconscious information conscious" (9). The student wants most of all to see the psychiatrist's mind and special technique in action. It is for this reason that the time devoted to demonstrations of initial interview technique has steadily increased over the years.

These didactic interviews are limited to 25 minutes in order to approximate conditions prevailing in the medical practitioner's office practice as much as possible. Patients are chosen at random from the Emergency Room as well as from the medical, thyroid, diabetic, neurological, and various other clinics. Rarely does a practitioner fail to be amazed at the amount of pertinent material the instructor is able to gather in such a relatively short time.

Formal lectures by attending and liaison psychiatrists in the Department have been gradually reduced from 25 to 14, while the space given to psychopharmacology has been tripled. Instruction in medical hypnosis is offered, as well as in suicide prevention, the treatment of alcoholism, and the problems inherent in drug dependence. Seminars are also given in child and adolescent psychiatry, the multiple sociopsychologic causes of delinquency, community psychiatry, emotional reactions to cardiac surgery, as well as in geriatrics, the attitude of physicians to the chronically ill patient and reactions of members of his family to the chronic invalid, problems of infertility, and related topics.

We have seen that practicing physicians made aware of psychiatric concepts and the significance of the doctor–patient relationship disseminate much needed mental health information and resources to their communities. We have also found that from fifty to eighty percent of all patients with psychiatric problems first consult their family physicians, who then have to make the important decision with respect to disposition, whether to refer such patients to specialists or to take a psychotherapeutic treatment upon themselves.

In an article entitled "What a Nonpsychiatric Physician Derives from a Course in Basic Psychiatry," Ben W. Aberman, who had participated in our course several years ago, remarked that "the course gives a new dimension to the practice of medicine. The old adage, 'Listen to the patient, he is telling you what is wrong,' is still very true medically. But just as true, as Theodor Reik put it, " 'Listening with the third ear' tells us what goes on emotionally" (10).

The ultimate goal of postgraduate education in psychological medicine is a significant change in attitude and outlook toward the doctor–patient relationship. We all know that attitudes are not changed by exhortation nor by logical remonstration alone. But it is astonishing that 125 years after Feuchtersleben's insights were published, physicians still believe that organic illness precludes emotional conflict and that an emotional or "functional" disturbance is only to be considered after thorough examinations and laboratory tests have failed to produce evidence of organic pathology. The artificial body-mind dualism is still alive in many physicians today and presents a powerful obstacle against acceptance of psychological medicine as a new discipline. The discipline may be relatively new, but the concept is as old as Feuchtersleben's conviction that all physiological and psychological phenomena form a unitary biological whole. "Wherever psychological abnormalities appear we are dealing with a mental disease; the cause of it is the psyche insofar as it expresses itself through the medium of a perceptive organ, and it is in the body insofar as the organ is the mediator for the psyche" (1).

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Teaching—or Preaching—the Behavioral Sciences

EMILY MUMFORD, PH.D.

More and more people have been stimulated to increased expectations of what physicians can do, and what they should be able and willing to do. Advances in medical science and technology and publicity about "breakthroughs" (sometimes premature) raise our hopes. Discretionary income and leisure have allowed time and resources to desire and to search for new and improved health services. The public has been led to believe that the medical profession owes it excellence in expanded areas. With interest generated and information extended, the public as well as the medical profession becomes more and more interested in what goes on at the source where new physicians are developed. We become increasingly concerned about what happens in medical schools where each year close to 10,000 new recruits enter into the moving experience, the transforming and stressful processes through which they become physicians.

Sociologists have helped medical educators to give medical students the dubious honor of first place on the list of professionals most studied, interviewed, observed, and discussed (1). Large numbers of the nation's most respected medical researchers, scholars, and clinicians attend to the development of students toward full professional stature. Curricula are devised and revised, committees meet and new methods are tried in the interest of reaching students or pleasing them or capturing their imagination. Huge investments in energy, personnel, and hard cash are devoted to the development of physicians. For example in 1969 there were 23,014 full-time faculty members in the country's medical schools (2). Viewed in such terms, one economist's claim is that the cost of taking "one high school graduate and turning him into a physician now exceeds $100,000" (3).

Teaching of behavioral sciences has advanced apace within medical education. According to a GAP (Group for Advancement of Psychiatry) report of 1961, "if the 1940's was an era of psychodynamic and psychoanalytic expansion, the 1950's can be considered the introductory period of the social or behavioral sciences" (4). Describing expansion of these programs, the report continued, " . . . today most medical schools in the United States have some behavioral science content in their curricula and research programs, with psychiatry providing the most consistent link between the behavioral sciences and other fields of medicine" (4).

The United States is not alone in this direction (5–8). "In the academic year 1965–66, all medical schools in Poland introduced sociology into the curriculum for medical students" (9). Previously, by an interesting bit of reasoning, the official view in Poland had been that such teaching "had no reason for existence in a socialist country where social factors harmful to health had supposedly been eliminated" (9, p. 428). Medical schools in Europe and in Latin America have also moved to include behavioral science material and courses.

The medical historian Sigerist once referred to medicine as one of the social sciences, but he didn't exactly start a trend (10). Others have reintroduced the idea as they notice relationships between medicine and social and/or behavioral sciences (11–12). It is not that some insights of behavioral science are new to medicine. Doctors have shown intelligent concern for the "total" patient, his emotions, his family, and occupational pressures, and his comprehension of his illness long before there was talk about status, role, and social correlates of some diseases (13–14). Indeed, debates about whether or where or when psychological and social variables should be considered in diagnosis and treatment sometimes recall the dilemma of the gentleman who had noticed no trouble managing his long beard upon retiring—until someone asked him whether he kept it outside or under the sheets and blankets. Moliere's *Bourgeois Gentilhomme*—enraptured to discover he had been speaking prose all along—also comes to mind.

What is new is the addition of specific individuals to speak for behavioral science within medical faculties. If they do their job well, students will gain clarity and comprehension of how different and how complementary the perspectives of the various disciplines actually are. They will learn how variables from each of several disciplines can be applied meaningfully and with new sophistication by the physician as he weighs probabilities in diagnosis and plans for therapy.

It is appropriate to discuss integration of the behavioral sciences in medical education in this volume. M. Ralph Kaufman has been a commanding spokesman for the physician's responsibility for comprehensive care of his patient, as well as for the need to keep in mind both psychiatric and social components in physical illness (15–21). He followed his precepts as a pioneer by developing a department of psychiatry that became, through its commitment and through the mechanism of an active liaison program, an integral part of a general hospital. With the opening of the new Mount Sinai School of Medicine, the liaison program was employed as a means for incorporating behavioral science perspectives in the learning experience of clinical clerkships.

Presently there is wide acceptance of the goals represented by the work of behavioral scientists, but there are still differences over the means for reaching them. Opinions vary over which disciplines should be included in social science, and which in behavioral, and whether social and behavioral science mean the same thing, and there is even more debate about where to put them in organizations and in curricula. The National Institutes of Mental Health usage of "behavioral science" includes biological sciences, psychology, and the social sciences (22). There is also the interdisciplinary view that sees behavioral sciences as collaborative efforts between sociology, anthropology, and social psychology (23). I will limit myself to this usage, but specifying sociology because I know more about it, and further I will relate the behavioral sciences to psychiatry, for it happens that psychiatrists have led medical-educational efforts to bring behavioral science meaningfully into the medical school (23).

A recent article on teaching the behavioral sciences in the *Journal of Medical*

Education observed, "With the exception of those programs which were initiated in a new medical school or in one which had completely revised its curriculum, there have been difficulties in obtaining necessary support, that is, provision of time, space, funds, and philosophical acceptance by the faculty" (24). Beyond the advantage in relative flexibility that a new program offers, it enjoys the potential of learning from the mistakes and experiences of others. Fortunately, it is the norm in medicine to share knowledge with colleagues.

The Russell Sage Foundation's examination of working relations between social scientists and clinicians informs us of many problems. The report mentions the social scientist who becomes a hermit, speaking a language no one understands or cares to learn. It also notes that people in different fields have sometimes incongruous expectations for what other disciplines are supposed to offer (25).

Thurnblad and McCurdy reviewed over 20 medical school programs in human behavior and wrote: "The addition of social scientists to medical school faculties may pose several questions: (a) the social scientist may be philosophically isolated from the medical faculty; (b) he must repeatedly justify his importance; (c) his contacts with other social scientists may become limited; (d) medical schools do not offer him senior positions, tenure, and salaries comparable with physician faculty members; and (e) the social scientist is not prepared in his graduate training to teach medical students" (24). Moreover students are bombarded with so much talk and such high expectations that they are sometimes pushed to selective attention, concentrating on what their institution conveys as most important and what they come to see as essential for the physician to attend to. They know they must master a body of knowledge. They are likely to be easily convinced that they must strive to be right in physical diagnosis and selection of therapies. But though they are also urged to recognize and acknowledge the patient's fears, his misconceptions about medicine, the social and economic implications of illness, and other data, it would often seem that these considerations are given more lip service than real service. Little wonder if lectures in this second area often fail to achieve their end when their directions do not receive consistent, daily, and multiple supports in actions and examples from the people the student seeks to emulate.

Two different attitudes of the physician can lead to a patient's justified perception that his doctor does not care enough about the social and emotional problems of the sick person. First, the physician can deny those aspects of patient's problems which he has been allowed to deny repeatedly throughout his training experience. A few lectures on the importance of social and emotional factors are a poor match to offset the sometimes urgent need for the doctor to deny problems that could threaten his emotional equilibrium and his self confidence. This is doubly so when the training experience encourages the developing physician to prosper through show of brilliance on teaching rounds, and perhaps even to be rewarded *least* when he has spent time with his patient, or when he has worked with a social worker toward solving a problem for his patient. Second, the physician may be aware of social and emotional components of illness and recognize these factors as relevant to treatment success, but then be convinced that someone else who specializes in these areas, not himself, should assume responsibility for seeing that something is done. Once the appropriate experts are requested, physicians with this approach may back away even further from the problems of coordinating such efforts for his patients.

Given these factors, behavioral scientists need to do more than preach in order to exert an impact sufficient to add knowledge that will be used and to deepen the student's conception of the enduring responsibility of the physician.

Many behavioral scientists lecture about how culture and social structure influence human beings in health and illness. Many of us can cite compelling evidence of benefits to a patient when a physician has taken such factors into account. Yet, I believe, that we ourselves do not sufficiently attend to these very matters we preach about. We sometimes act as though we have forgotten both the psychological and sociological factors which must be managed if students are to accept and to use what we teach. We say the social structure is important, but we sometimes act as though it is not. We say that the climate, the culture in which a person functions may exert large influence on his perceptions and his choices among alternatives. But too often we let our case rest with argument, forgetting how important the school climate, the daily actions that are reinforced or ignored, and the example of physician role-models can be. If such factors can support or vitiate classroom efforts, we should attend them diligently.

In medical school tables of organization, the behavioral and social sciences are sometimes included as an extension and adjunct to psychiatry, sometimes as a part of community or preventive medicine. Behavioral scientists are at times introduced into curricula through internal medicine, sometimes through obstetrics or pediatrics. A third, relatively new major organizational arrangement includes a separate department of behavioral science in the medical school. The separate department plan has some advantages in recruiting a strong department when it can offer some professional autonomy, tenure, salary, and positions. If such a department is centrally located in the medical school, it provides many chances for behavioral scientists to influence hospital and medical school planning. They can establish active teaching programs in the school of dentistry and the school of nursing and allied professions, and they can train graduate students in medical sociology.

The teaching program of such a vigorous department can offer advantages of well run, small-group seminars. The arrangement also seems to contribute to effective use of behavioral scientists by faculty members in other departments —a powerful assist in confirming the uses of behavioral scientists.

Students in such a setting have pretty good chances of seeing physicians who are most knowledgeable about these disciplines and who sometimes consult with behavioral scientists. In one school where I visited and interviewed, some faculty members seemed convinced that their students emerge less cynical, more compassionate, and probably more aware of social and emotional factors in illness than students from some other places. A few faculty members said they believed that histories done by residents from their own school were generally more full and more comprehensive of relevant social and emotional material than histories done by graduates of other places.*

But though the separate group of behavioral scientists may have high morale, and others on the faculty seem to feel they all must be doing something right, students at this same school where I was able to interview refer to "The BS Course" with some malice. One said, "It was my opinion all the way through that it was primarily knowledge which should have been picked up in high school and college. I was a psychology major and also had a good deal of sociology." He later added that while the lectures didn't add much, the seminars—where they had a chance to discuss problems with other students—"were okay."

Another student said, "It is hard to teach people to be human beings, but it is very necessary . . . They emphasized that the patients are people in that course, but they should also emphasize that the physicians are people, too. I think we would all agree with their goals, but we're not sure about the method." He later said, "Also, there is some question about whether you can teach common sense to someone who is 21 and in medical school . . . I think it would be better if you had sociology and psychology as requirements for entrance into medical school. We should have it, but earlier." He mentioned informal evening get-togethers with an obstetrician, whom the students admire, as perhaps more useful than a group "run by somebody like a statistician!"

Students describe the language of behavioral scientists as jargon. One said, "The jargon can be overbearing . . . They start talking about role theory and role this and role that . . . The lectures were worthless to me." He mused a second, then added, "The course is not an imposition. Maybe you need a course like that which you do not have to work very hard on. Some of the discussions in seminars and lab were interesting. But a lecture on the age-sex pyramid of the Hopi! Who needs it? Also, the problem was that they talked about their own research. You have to use your slides for something, I guess." As he warmed to his subject, one said, "I'm trying to think about the parts that were good, but I cannot think of anything."

Faculty members in other departments made some of the same criticisms and with some of the same examples about "all that role stuff." The similarities suggest a degree of consensus, influence, or remarkable coincidence. Here, too, people agree with the goals and need for the perspectives of behavioral science, but they question the timing and are irritated by the jargon.

In his review of behavioral science programs, Susser writes about one medical school, "The medical school (which does have a separate behavioral science department) . . . is probably better served in the behavioral sciences than is any other medical school. But their segregation within a department may cause a rather smaller impact on medical students than was hoped for" (26).

A second organizational arrangement is committee responsibility where physicians of several specialties run a seminar. This can lead to fewer student complaints about being taught by a lot of people who "aren't even physicians." Also, it may cut down on static about jargon. If an occasional outside behavioral scientist is invited for a lecture or two, chances are that this presentation could lack "relevance," but it may not disturb anyone too much. This structure seems to lead the pair, or the group, or representatives of the medical specialties to speak for various behavioral sciences. When this happens, there are probably better chances that students will see the relevance of whatever behavioral science material the physician notes. Also, having only physicians teach the student provides more medical role-models rather than so many others, like the Ph.D. physiologist, geneticist, sociologist, psychologist, and anthropologist. This may be to the good, but this direction leads to its own large problems.

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* The resident, instead of continuing and reinforcing educational gains the medical school makes, may vitiate them. Probably a major force in the learning experience of medical students—the interns and residents—is seldom discussed as teachers. Their impact on students awaits adequate study.

One ambitious two-year course in which a group of physicians attempted to cover archeology, ethology, sociology, and many others, came to the end of the first year in what one of its key members referred to as a "state of disaster." Beyond the obvious limits when one discipline speaks for another, there is a second disadvantage when a committee of physicians elects to divide up the behavioral assignments for coverage. The process may, by example, convey a message the educators did not intend. When the physician "covers" sociology, or psychology, or any specialty outside his own—in one or a few lectures—students may assume that they "know all any doctor needs of all that stuff." This is particularly a problem around disciplines that deal with social and emotional factors where the professional from another discipline turns Descartes inside out and claims, "I know because I am." Or there is also the possible consequence of Pogo's version of Voltaire: "I don't understand what you say, but I'll defend to your death my right to deny it."

Most psychiatrists have had experience with someone, whether physician or laymen, who assumes he knows as much as he needs to about psychiatry and thus does not bother to seek a consultation. One resident in medicine complained about interns whose training he considered inadequate: "They don't know enough yet to know when they don't know enough." Some behavioral scientists have had this impression at times when various medical specialists dismiss material from the behavioral science as "only common sense" or "not relevant." A first duty in education is to open the mind to what is yet to be known.

An internist who presently runs what appears to be a fine course is probably accurate in his conviction that *one* man must be responsible for presenting a good course and for recruiting behavioral scientists for selected discussions which are appropriately timed for the particular stage of the students' development.* He and others suggest that psychiatry and preventive medicine each are somewhat disadvantaged in the eyes of the student searching for the *Doctor*. The Ph.D. behavioral scientist is even worse off. The more prestigious the medical spokesman in such courses, the better. The more charismatic he is, the better, and if he is an internist, too, it's better than better, it's the best.

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* A report on one interdisciplinary course in behavioral science for first-year medical students emphasizes need for "...substantial preparation by the teachers prior to each class meeting. It is incumbent upon them to assign appropriate readings and to impart the necessary background theories and concepts together with the research evidence and the logical basis for their theories or concepts. Otherwise the student passes between the

A third arrangement places most of the Ph.D. behavioral scientists in departments of community medicine. If the department has a vigorous program that encourages close collaboration between M.D. and Ph.D., behavioral scientists can receive effective support for active teaching and research which complement each other. There is some risk that some students will come to see behavioral sciences as pertinent only for community-oriented efforts. But the arrangement offers advantages for recruiting some behavioral scientists who require data and research facilities for their professional development and interest.

The presence of a group of behavioral scientists who collaborate over research also enhances the probability for effective collaboration in teaching.

The fourth arrangement that places the behavioral sciences in the department of psychiatry can also provide the non-M.D.'s with a medical base. If their patron is sufficiently strong and interested, some of the problems of recruitment and morale of behavioral scientists in medical school can be kept to a minimum. This arrangement probably works to hold behavioral science emphasis on clinical work—on comprehensive care of the patient. At all times behavioral scientists of a department of psychiatry should complement the work of behavioral scientists in other departments, and it may be that maximum effectiveness can be achieved where behavioral scientists are assigned to work in several different specialties but still have opportunities for exchange and research with colleagues in their own discipline through one department.

Managed well it is possible that the alliance of a Ph.D. behavioral scientist with a specific clinical department, such as psychiatry, can reinforce the psychiatrist's teaching at the same time it demonstrates the clinical applicability of the behavioral scientist's contribution. In a hospital with active community mental health programs, this arrangement makes even more sense.

Presenting behavioral science via a department of psychiatry introduces the larger subject of teaching psychiatry in medical schools—an area that has received much attention. A half a century ago psychiatry had an average of 30 to 40 hours in the entire curriculum of many schools. By 1966 most departments were assigned 300 or more hours. A joint committee of the American Association of Medical Colleges recommended some ten percent of the 4,000 hours of the total medical school hours should be allotted to psychiatry, and the committee affirmed experience with psychotherapy as basic for medical practice. In light of this directive—and the trend in medical schools—both method and content of these courses need careful consideration.

Students' views of courses in psychiatry suggest room for improvement of either structure and content of courses, or improvement of psychiatrists, or

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Scylla, or mere authoritative assertation which simply propagandizes him, and the Charybdis of the uninformed bull session or even 'wild' group psychotherapy" (27).

students, or all of these. Critical comments could also reflect great expectations and increasing desire among students for what should be learned in psychiatry. One resident put it: "My specialty is radiology. My experience as an intern at ——— leads me to suggest that medical students be given more instruction than is usually given in the management of the dying patient and the emotional support of their families. This area along with the subjects of suicide and sexual difficulties tend to be 'sidestepped'."

Student images of specialties do change in some schools, and not to the advantage of psychiatry, which in one school ended up with lowest rating except for dermatology (28). This is of interest because *college* students do not put psychiatry down so far. At one college they viewed psychiatry more positively than did preclinical students in the affiliated medical school. A research team at the University of Oklahoma sums it up, "It can be seen . . . that as medical knowledge and experience increase, the image of internal medicine becomes more positive whereas the opposite is true for the image of psychiatry" (29). Wives of medical students in one school follow the same pattern. Clinical students' wives rate each of 6 specialties lower than do wives of preclinical students. But the down-grading is "notably so for psychiatry, pediatrics, and obstetrics-gynecology" (30).

It is reasonable that the psychiatrist would lean toward unconscious factors in explaining students' disaffection with psychiatric courses. Each discipline legitimately employs its own perspective first in explaining phenomena. Moreover, resistance of the student to psychiatric material is a salient factor that nonpsychiatric specialists tend to overlook when they criticize teaching in psychiatry. The material presented by psychiatry also is more subject to distortion by students—a condition that leads one educator in psychiatry to urge that lectures be followed by small group seminars where misconceptions would have a chance to be corrected. But in addition to these factors, we should consider others that may contribute to a decline in some students' respect for psychiatry through their years in medical school. One psychiatrist cites a lack of coordination between different psychiatric courses given to medical students (31). Psychiatrists are also criticized for being too accepting of inadequate case presentations, too undemanding, and generally too relaxed about their teaching responsibilities (32). One student reported about psychiatry, ". . . the second year course was a good idea but it didn't work. They give you these mimeographed sheets. They are not printed well and you can't read anything on them. Those damn sheets. They have the most complicated syntax. The guy who wrote them must have had a motor aphasia" (31).

Nobody can guarantee that students' reports of interest and enjoyment is a gauge of meaningful learning and education, though we sometimes assume it is. Students can enjoy the "bull-session" type of teaching and dread courses where they are taxed and probed, and yet they may later report that they learned a lot in the course where they were pressed. There is a wish that enjoyment and learning necessarily "go together." But that may be no better proved than the former conviction that absence of enjoyment "went with" learning and all manner of human improvement. Even expressed interest in courses can vary, depending on *when* the student is asked. "At Yale, students in the preclinical years received a course in human ecology and rated it highly at the time. In their final year the same students were asked to recall and again to rate the ecology course they had received in their preclinical years. The ratings showed a large shift toward unfavorable opinion" (26).

The psychiatrist with his halo slightly askew is not infrequently a subject of humor, sometimes derision, within the medical profession, and this does influence students' attitudes toward psychiatry. When the medical student never sees the internist consult a psychiatrist, or when he observes that upon consultation the psychiatrist doesn't help, that student is learning something about psychiatry in medicine. But he is probably not learning what either the internists or the psychiatrists on the faculty hope for when they plan the curriculum and state school aims. Admonitions once a week are poor competition for a multitude of daily actions when the two sources convey competing messages.

I believe it was Whitehead who said, "We think in generalities, but we live in detail." Because students learn in unplanned, as well as planned ways, some conscious attention may well be paid to the nature of exchanges when faculty representatives talk across disciplines. The Mount Sinai tradition of active liaison between psychiatry and each of the other specialties provides a good base for behavioral science exchange. The fact that residents, as well as attending physicians work in liaison service also bodes well for student learning about effective consultation in the hospital.* It is an aspect of the hospital which should be *used* for teaching. Students often take interns or residents as role models—the physicians they emulate. Where this happens, the residents' actions can be instrumental in supporting or in undercutting directions that the faculty is trying to encourage. It is probably essential to attend to the residents and measure the level of their comprehension of psychiatric and behavioral science material before students are assigned to work with them.

Meaningful consultation is, of course, not guaranteed by good will and good intentions, though a measure of these may help. Consulting skills are probably best developed where a psychiatrist has enough experience working within one specialty so he can make recommendations within the realities of that specialty. The hospital where a body of attending psychiatrists and their residents have regular assignments on specific other services will afford many chances for students to see capable consultants in action. An established and active psychiatric consultation program in the hospital increases the chances that the student will encounter other specialists who, having sought consultation appropriately, then attend to the consultant's discussion. Such training of residents in consultation may improve the unfortunate situation Garber noted from his sample of physicians who were asked which sources gave them most knowledge of psychiatry. Psychiatric consultations were a poor last; eighty-three percent of the GP's didn't check this source at all. Next to this least-mentioned source came medical school (34).

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* The benefits of giving general hospital experience to psychiatrists are characteristically well expressed by Beaton: "... my first order of the day is that our new-fledged psychiatrist be put into a general hospital for at least a part of his every working day, even if he has to be tied there" (33).

If the "injection" of psychiatry and behavioral science is to "take" with medical students, they must see its relevance for themselves (35). They can see this by example, by precept, or by reason and argument. They may see it most clearly by experience, for example, when the student has noticed an important emotional or social component of the clinical picture and is praised for his insight, or when a physician he esteems calls him up short for overlooking these matters. Motivated to do well, students, as others do, look for cues to let them know how well they are doing, and they are very quick to catch on to what brings favorable or unfavorable notice on each service (36–38). Experience, as well as teaching, through medical school, internship, and residency can condition the physician to a pattern of routinely ignoring certain variables or of customarily giving them consideration.

Students come to "feel like" physicians through finding they can perform successfully as doctor to patient (39). The early experiences that help them toward that important feeling can have special import (40–42). Therefore, psychiatry may do well to attend carefully and to seize opportunities where students will see first hand that they *can* bring some benefit to any patient who has an emotional problem. The average turnover rates in surgery and medicine provide relatively frequent chances for medical students to see a patient through illness and recovery and learn from that. The student on surgery and on medicine who is helped to recognize and work with pressing social and emotional factors on behalf of his patient has good chances of seeing the benefits of such efforts.

Castelnuovo-Tedesco's survey of nonpsychiatric house staff members reports that ". . . in most instances the student had not had the experience of beginning or completing the (psychiatric) patient's treatment" (43). Fifty-seven percent of these respondents said that the patients they treated on psychiatry "had remained the same" (43). As one chairman of a faculty in psychiatry said, "The student must come out feeling that they have mastered something. They have to go through a process of getting into the ward. They have to have time to learn to deal with their anxiety."

With the rapid advance in all the medical-relevant sciences and the enlarged lay expectations for what physicians should be able to do, the medical educator's task becomes increasingly more complex and difficult. It becomes less and less feasible for the physician to expect that he can give the student all the specifics the future doctor will need for a lifetime of practice (44–46). By the same token it becomes more urgent that the developing physician learn the habit of meaningful consultation, becomes committed to the need for continuing education, and accepts a sense of professional responsibility for his patient, as a social-emotional-physical being.

As high school science is upgraded, there are more college, advanced placement, and honors courses (47–49). Faculties must plan for new kinds of student bodies. Some arrive competent, perhaps advanced in one science, some in others. More free time and more elective time on curricula helps to meet the challenge of advanced training, and of increasing specialization and differentiation of medical careers. Electives can also provide systematically for faculty influence on student development through small groups with shared interest, and also can allow students to advance up to the level of their capability.

The physician-educator of 50 years ago could concentrate on content and be reasonably assured of two things. First, he would continue ahead of his students in the sciences he was teaching. Second, his experiences in treating patients through the years would be of interest to his students, most of whom hoped for a private practice.

The man who teaches an advancing science today has a greater challenge. His students will go into more differentiated careers. He cannot rest with conveying facts, and believe the student will have the information needed for a lifetime of practice. The educator today must sow seeds of discontent with present knowledge, while at the same time he is obliged to give the student a foundation secure enough for effective action. The behavioral scientist shares these problems with others who teach medical students. But he has difficulties of another order which must be managed. Groups of medical students, unsure of their position in medicine, can be expected to respond negatively to any situation, and to any person who does not help them to feel more like doctors. Being taught by a Ph.D., being given material that students are not ready to accept as something a doctor *has* to know, may be the kind of experiences such a group discredits. Such material is in special jeopardy if its value and its appropriateness is not reaffirmed consistently and effectively in the swift and compelling action to which the student is exposed as he struggles to become a physician. Since students cannot always be depended on to know what is important, or to know how much they do not know, it is up to the educator to attend carefully to arranging the structure of learning experiences as well as the material and its sequence so that the relevance of it all has the best chance of being perceived by the students while they are still in a fairly plastic phase of their development. Beyond that, part of the necessary function of sociology in the medical teaching enterprise may be to reiterate to colleagues the importance of climate and structure for development of the student physician.

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RESEARCH, 1945-1970

SEYMOUR ROSENBLATT, M.D.

Justice would be better served if all the original and often seminal contributions of the members of the Department of Psychiatry of The Mount Sinai Hospital could be cited and discussed in this chapter. Unfortunately limitations of space and the need to present a coherent and comprehensive account compel me to ignore the greater part of the more than 500 papers that have been published during the period of Dr. Kaufman's stimulating and inspiring leadership, and to concentrate instead upon a few representative examples. In the interest of succinctness and brevity I have omitted from this chapter any discussion of research reported elsewhere in these essays.* To those many others whom I have failed to mention I offer my regrets. Much of this review is based on summaries of work provided by members of the department without which my task would have been immeasurably greater. For their time and effort I express my gratitude.

A perusal of the department bibliography since 1945 not surprisingly mirrors the thrust of psychiatry over this past generation. Hence the earlier papers, reflecting the neurological training of many members of the staff, were clinical neurological studies. With the flowering of psychoanalysis and psychoanalytic psychiatry in the postwar years, and as a result of the training in psychoanalysis which many members of the department received, there occurred a conspicuous growth of the number of papers possessing a psychoanalytic orientation. In light of Dr. Kaufman's own rigorous training in that discipline and of his strong commitment to the importance of psychiatry in the general hospital, it was not long before psychoanalytic concepts and principles were applied to an understanding of many aspects of ill health, hospitalization, and convalescence, with particular emphasis on psychosomatic conditions. Obviously, a comprehensive review of his own vast contribution to the psychiatric and psychoanalytic literature is quite out of the question here. (A list of his extensive bibliography will be found elsewhere in this volume.) Instead, somewhat arbitrarily, perhaps, I have selected three dissimilar clinical studies in which he participated.

The first, conducted jointly with Drs. Edward D. Joseph and Samuel Peck, described the successful removal of the skin lesions of a patient with neurodermatitis by hypnosis, which result, however, was followed by the abrupt appearance of a florid psychosis necessitating electroshock therapy. This case provided a dramatic example of the replacement of one symptom by another and of the consequent potential danger of injudicious symptom removal. The second paper, written in collaboration with Drs. David Kairys and Abraham Franzblau, concerns the complex and widespread emotional impact of the ancient and traditional institution of ward rounds. Out of this study of the interaction between physician and patient came some very pertinent recommendations to the medical and surgical staffs. The third study, published jointly with Drs. Samuel Lehrman, Samuel Tabbat, Leonard Weinroth, Stanley Friedman, and Abraham Franzblau again dealt with the emotional reactions of the hospitalized patient, notably the response of the latter to the fact of admission to the hospital. A sample of 253 persons studied within the first twenty-four hours of admission to the medical ward revealed an incidence of diagnosable psychiatric disorders in over two-thirds of the cases. Among patients with psychosomatic or functional conditions the incidence was even higher.

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* E.g., Dr. Alvin Goldfarb's rich and far-reaching studies in the field of geriatric psychiatry, Dr. Gustav Bychowski's inquiry into the role of poverty on mental health, Dr. Paul Friedman's important research in suicide, Dr. Richard Frank's extensive observations on adolescent children, and the work of Dr. Milton Sapirstein and his coworkers on the psychologic problems arising in industry and various professional groups.

These three studies illustrate the wealth of clinical material and the rich reservoir of new insights and knowledge residing in that borderland between psychiatry and the rest of medical practice—the borderland which at The Mount Sinai Hospital has been the province of the liaison psychiatrist. It should be emphasized, moreover, that for the most part the contribution of the latter to research has been made without either financial support or assistance, itself a measure of the enthusiasm and dedication of the attending psychiatric staff during the past twenty-five years.

One member of the department whose several liaison assignments have resulted in an especially productive and varied output is Dr. Louis Linn. Working initially with Dr. Irving Goldman in the Ear, Nose, and Throat Clinic he undertook a psychiatric study of patients undergoing rhinoplasty. This experience served to impress upon him the usefulness as well as the validity of Schilder's concept of "body image," which subsequently became a recurrent theme in his later work. As liaison psychiatrist on the neurological service, with Dr. Edwin A. Weinstein, he participated in the development of the Sodium Amytal® test for organic brain disease. Later he became interested in the psychiatric consequences of eye surgery, especially cataract extraction on older persons, and he investigated the nature and significance of the organic mental syndromes precipitated by electroshock treatment. This ultimately led to a paper on the reticular activating system, one of the first theoretical communications in which an attempt was made to integrate psychoanalytic concepts with neurophysiology. With the development of psychotropic drugs in the 1950's, Dr. Linn became interested in determining how mental processes might be affected by these substances. His extensive liaison work provided him with a comprehensive view of many aspects of hospital psychiatry and resulted in the publication of a classic work, *A Handbook of Hospital Psychiatry*. As with so many other members of the department, his current direction has turned to the burgeoning field of community psychiatry where he has continued to explore and write extensively.

Liaison psychiatrists on the surgical service have similarly made a number of contributions. Dr. Victor Rosen published an important paper revealing the relationship between denial—both by the patient and the surgeons—of the obvious need for amputation of a limb and the development of psychosis. Dr.

Bernard C. Meyer has written on the subject of chronic ulcerative colitis and on intestinal stomas. With Dr. Albert Lyons of the Department of Surgery he published a detailed account of a case of rectal cancer in a young man which provided significant insights into the medical, surgical and psychiatric problems created both by the disease and by the consequences of its cure, notably the colostomy and organic sexual impotence. With Drs. Fred Brown and Abraham Levine of the Department of Psychology, Dr. Meyer subjected a series of patients, before and after surgery, to the House-Tree-Person Drawing Test. The latter proved to be an extremely sensitive instrument for the detection of attitudes and reactions of individuals faced with the stress of surgery who often enough failed to reveal any such manifestations under other conditions. With Dr. Richard Blacher and Dr. Brown, Dr. Meyer undertook a somewhat similar study of patients undergoing mitral commissurotomy. A particularly significant discovery was the occasional occurrence of what the authors termed a postoperative traumatic neurotic reaction, caused apparently by the effect of succinylcholine in masking the degree of the subject's consciousness during the surgical procedure.

Another group of individuals who are apparently often far more lucid and aware of their surrounding than is commonly believed, are postoperative patients in the recovery room whose mental and emotional reactions became the object of a study by Dr. Charles Winkelstein, Dr. Blacher and Dr. Meyer. It was then only natural that these three collaborators subsequently sought to establish whether patients in states of deep surgical anesthesia are able to register auditory stimuli as has been claimed by some investigators.

Dr. Meyer has also contributed a number of papers on the doctor–patient relationship in surgical practice with particular emphasis on the vexing problem of what the patient should be told about his illness. The psychological aspects of death and dying have been of concern to other members of the liaison staff as well, notably Drs. Richard S. Blacher, Charles Winkelstein, Lawrence Roose, and Samuel L. Feder. Related to this subject is an inquiry undertaken and published by Drs. Meyer and Blacher concerning the utilization of a variety of creative thrusts, both biologic and artistic, as a means of warding off suicidal impulses by a chronically depressed woman.

From the foregoing it is clear that just as the liaison psychiatrist may exert an influence on the thinking and attitudes of another clinical service, so may the latter stimulate the interest of the liaison psychiatrist. Such a reciprocal interaction is particulary evident among the liaison psychiatrists who have been attached to the Obstetrical-Gynecological Service. In that capacity Dr. Marcel Heiman was prompted to publish a number of important papers dealing with the psychological aspects of fertility, uterine bleeding, adoption, abortion. During the past three years Dr. Stuart Asch has become aware that pregnancy is a condition in which the psychological construct of an "introjected object" attains the property of a physical reality. He observed moreover that reactions of anxiety during pregnancy depended on the different physiological manifestations of each state, noting that anxiety often increases at nineteen to twenty-one weeks when "quickening" appears. At this point a patient may become confused when the "fantasied" introject is perceived as real. It was also noted that there were probably many instances of mothers hurting or even killing their babies as a result of projection and displacement of the intrapsychic elements in a postpartum depression, as an expression of a desire to destroy something she feels as the "bad part of herself". Under conditions where this "bad" part is displaced onto the newborn, it can lead to assault or infanticide. Recently Dr. Asch has extended this study into a wider investigation in collaboration with Drs. David Shapiro and Nathaniel Karush and the Medical Examiner's Office of New York. They are investigating the incidence of postpartum depressions associated with crib deaths. An important development of his work results from his studies of the subject of identification and its relevance to the incorporation by the individual of the social values, behavior, permissions and prohibitions sanctioned by society—i.e. the development of the super-ego. He observed that the superego structure is not fixed but requires constant support by outside pressures. Without such consistent reinforcement, superego functions tend to erode and antisocial behavior results. This hypothesis, developed from basic psychoanalytic concepts, may have relevance for the crisis of youth today where, as has been suggested, weakening of superego reinforcement is perhaps a factor in the anarchic attacks on all social institutions. The implications are profound and may offer a direction for a society challenged, on the razor-edge of the moment, to strike a balance between the values of yesterday and tomorrow.

Despite the impressive contributions to an understanding of many psychiatric and psychosomatic processes which were facilitated by the rigorous psychoanalytic training of many members of our department, it soon became apparent that the one-to-one treatment modality could hardly meet the tremendous demand for psychiatric therapy in the inpatient and outpatient departments of a general hospital. Hence, experimentation with other forms of therapy was instituted, but, in the tradition and philosophy of medicine, new approaches were slowly evolved and were based upon knowledge obtained from previously tested methods. This trend can be best exemplified by the contributions of Dr. Aaron Stein in his careful studies of group psychotherapy, which are recorded elsewhere in this volume. Dr. Stein cautiously extended his studies of group interactions as a therapeutic tool and has provided much of the solid foundations of group therapy principles which are utilized today in this form of treatment. The need for such conservative evolution in medical practice, moving from raw data to testable hypotheses to sound therapeutic principles, is especially urgent in the present day explosion of unscientific group therapies. Another investigator of group therapy in our department has been Dr. Peter Laqueur who was one of the first to initiate multiple family therapy with the families of schizophrenic patients. He has shown that one can extrapolate from general systems theory to the processes of multiple family therapy and produce desirable outputs in an effective and efficient manner under constantly varying circumstances. His application of general systems theory to a specific branch of psychotherapy indicates that psychiatry itself is an open system utilizing stimuli and information from many sources and feeding back an effect in its therapeutic output.

Still another departure from traditional psychiatric practice designed to meet the need of treatment for larger numbers of patients was the establishment of partial hospitalization. Many psychiatric patients, although ill enough to require treatment in a psychiatric facility, do not require 24-hour hospitalization. The Day and Night Center at The Mount Sinai Hospital has been described elsewhere in this volume by the chief of the division, Dr. Samuel L. Feder.

The introduction of technical innovations and of neurophysiological and biochemical instruments has facilitated the acquisition of new data and has provided some striking opportunities for integrating the latter into the framework of psychoanalytic theory and thinking. Thus, in a multidisciplined study, which included psychoanalytically-oriented therapy of a patient with a gastric fistula, Dr. Sidnay Margolin and his coworkers—and later Dr. Aaron Stein—furnished new and important findings in the field of gastric physiology, thereby complementing the earlier classic observations of William Beaumont and of Wolff and Wolf. Similarly, using radioactive iodine determinations, Dr. Hans Kleinschmidt and his coworkers were able to explore the relationship of abnormal thyroid function to underlying personality structure and mental conflict. Dr. Kleinschimdt indeed was one of the first to reject the popular concept of specificity in terms of personality or conflict situation in psychosomatic conditions. He observed that the "traumatic" events preceding the onset of thyrotoxicosis were not outside the realm of the patient's usual life experiences. He found, moreover, an intimate correlation between thyroid imbalance and affective tone—predominantly depressive. In another study, using protein-bound I^{131} plasma level determinations, he showed that thyroid activity was autonomous in anxiety states in psychiatric patients.

Using tachistoscopic (i.e., fractions of a second) exposure to visual stimuli, Dr. Charles Fisher began his work in the department in 1953 with a replication of Otto Pötzl's classical experiments on the role of subliminal perception in dreams. Dr. Fisher found that percepts which were subliminal were nevertheless registered and extensively utilized in dream formation. He also showed that images produced in the waking state could utilize subliminal percepts in much the same way as dreams. As an aside, it should be stated that the ability to influence drives and thinking by subliminal perception was seized upon at that time by commercial interests who saw it as a way of exploiting it to influence consumer choice. The implications go far beyond soap sales and over a decade ago this form of "mind control" was banned by state and federal authorities. A number of carefully controlled studies were carried on by Dr. Fisher which supported the contention that subliminal perception and registration were genuine phenomena. For several years, beginning in 1959, a series of investigations were carried out, in collaboration with Dr. William C. Dement, utilizing a new rapid eye movement (REM)—electroencephalographic technique for studying sleep and dreaming. Dr. Dement, working with Dr. N. Kleitman in Chicago, and others reported on the fact that a stage of sleep existed in which dreaming occurred and which was characterized by rapid eye movements, low-voltage, fast activity of the EEG, and muscular relaxation. Drs. Fisher and Dement observed that dream deprivation experiments induced by repeated awakening at the onset of the REM period brought about an extensive suppression of the cyclically recurring REM periods and they studied the effect of this suppression. The REM suppression method now has had many applications in man and animals and is one of the more important techniques for investigating various aspects of the physiology, psychology, and biochemistry of sleep and dreaming. Additional work by Drs. Fisher and Dement, with the collaboration of Dr. H. Roffwarg, concerned itself with the dream-sleep patterns of neonates, infants, children and adults. It was shown that REM is at its height in the neonate, taking up 50% of the sleep time. That REM sleep occurred in infants indicated that it is a neurophysiological phenomenon which probably only secondarily, in later stages, became associated with dreaming in symbols and pictures. Studies of nocturnal sleep of narcoleptics demonstrated that narcolepsy is essentially a disturbance of the mechanism of REM sleep.

An important discovery made by Dr. Fisher, with the collaboration of Dr. Joseph Gross and Dr. Joseph Zuch, was the finding that REM sleep is associated with a cycle of penile erection. This finding had important implications for psychoanalytic drive and dream theory and especially for the implications of the activation of the sexual drive during dreaming. Penile erection is but one manifestation of the marked autonomic activation during REM periods. It was also shown that the erection cycle is present from birth to extreme old age and occurs in lower forms of animals. Another important investigation carried out in Dr. Fisher's Sleep Laboratory by Dr. Stanley Friedman has been the demonstration of rhythmic, diurnal oral instinctual drive cycles in man which appear to be the extension of the nocturnal REM cycle during the day.

For the last several years an extensive study of the psychophysiology of nightmares has been under way. The group working with Dr. Fisher has confirmed the findings that most severe nightmares develop out of the deepest stage of nondreaming sleep (stage 4) and are a unique and singular phenomenon. Unlike most reported nightmares which are REM anxiety dreams of varying degrees of intensity, the true nightmare is relatively rare and represent a pathological symptom of obscure etiology. One of the important practical findings has been that stage 4 nightmares can be almost totally abolished by the administration of diazepam, which has the property of markedly reducing stage 4 delta sleep. This is a safe drug and thus appears to be a useful treatment for this type of nightmare. Prolonged suppression does not appear to cause any ill effect. The REM dream appears to play a special role in muting traumatic anxiety. A desomatization process seems to be an inherent part of the REM period, apparently serving the function of muting the autonomic concomitants of anxiety and thus helping to maintain REM sleep. Until recently the work of the past decade has strongly suggested that REM sleep and dreaming were necessary psychobiological processes. Recent work has tended to throw some doubt on this. In a recent report Dr. Fisher and his group have confirmed that monoamine inhibitors can bring about total suppression of REM sleep for periods of many months without undue psychological or behavioral effects. This phenomenon is now under intensive exploration.

My own research studies started about a year after my residency at The Mount Sinai Hospital when Dr. Kaufman allotted funds to purchase a photofluorimeter for the analysis of catecholamines, and Dr. Harry Sobotka, Chief of the Department of Chemistry, made laboratory space available. This marked the beginning of a close collaboration, lasting over a decade and continuing today, with Dr. Jacob Chanley, Associate Professor of Biochemistry. Through the generosity of the Mack Foundation, the department will have its own laboratory which is presently under construction on the ninth floor of the Klingenstein Clinical Center.

The purpose of the study was to measure changes in blood-brain-barrier permeability to norepinephrine after electroshock treatment. At that time, the hypothesis was being established that a deficiency in norepinephrine in the central nervous system may be a concomitant of depressive states, primarily endogenous depressions. It was speculated that electroshock treatment altered the permeability of the blood-brain-barrier, permitting an increased access of circulating norepinephrine to the hypothalamus and other subcortical centers. The first study was carried out on dogs who received a typical clinical course of electroshock therapy. We observed an almost three-fold increase in the penetration of norepinephrine into the spinal fluid. The next series of studies involved the development of a technique for analyzing the metabolites of norepinephrine in human subjects. It was known that infused radioactive norepinephrine entered the norepinephrine stores of the sympathetic nervous system and was released along with endogenous norepinephrine during sympathetic nerve activity. Since it was a simpler task to investigate the metabolites which are radioactive than those that are not, we began to investigate tritiated norepinephrine metabolism in man. Our initial work with Ronald Fecher concerned itself with the development of laboratory methods for analysis of all the radioactive metabolites of norepinephrine. When this work reached a satisfactory degree of reliability, we then turned our attention toward the affective disorders. We observed that the proportions of various metabolites of norepinephrine differed among a number of subtypes of depression as compared to normal controls but were not different when normal controls were compared with schizophrenia and involutional depression. We observed that manic-depressive, depressed subjects excreted a greater proportion of normetanephrine after infusing tritiated norepinephrine than did patients who were diagnosed as reactive depressions. This study was then extended to more detailed examination of the changing patterns of norepinephrine metabolism in a group of manic-depressive depressions and subject with other types of depression. The original findings were confirmed and one of the conclusions that we were able to draw is that the altered metabolism found in certain depressive states, rather than being caused by a diminished store or supply of norepinephrine, might be due to a decreased sensitivity of adrenergic receptor structures to normal amounts of norepinephrine. This hypothesis has been confirmed by others using different methods to measure the sensitivity of adrenergic receptor structures to infused norepinephrine in depressed subjects. It now appears that there are depressions which are associated with some alteration in noradrenergic physiology and these are to be distinguished from others in which this disorder is not found. We then investigated the effect of a variety of psychotropic drugs upon the metabolism of norepinephrine in human subjects. We found differences in the effects of phenothiazines, reserpine, tricyclic drugs, and monoamine oxidase inhibitors on tritiated norepinephrine metabolism. Currently we have been developing a laboratory procedure to monitor the dosage of tricyclic drugs in the treatment of depressions, in contrast to current practice wherein drug treatment of depression is purely empirical and the dosage is regulated by clinical observation. One drawback of this latter method is the existence of a time lag between the start of tricyclic drug administration and the onset of antidepressant effects. We have speculated that it may be possible early in the treatment to measure the pharmacological effectiveness of a given dosage level of tricyclic drugs on the sympathetic nervous system via the changes induced in tritiated norepinephrine metabolism. This would permit an early determination of optimum dosage as well as an early evaluation of potential effectiveness of a given agent.

For the past three years we have been engaged in a study with Dr. Alvin Goldfarb of the effects of lithium carbonate treatment on manic-depressive disorders. Lithium is markedly effective in reducing a manic state without producing the side effects encountered with phenothiazines. It has a remarkable prophylactic property, namely in preventing recurrences of mania, when given in maintenance doses. It is also proving effective in preventing or significantly attenuating the course of recurring depressions as well. Lithium therapy is perhaps a harbinger of a new phase of psychiatry—the prevention of disease by subtly altering basic molecular events, thereby providing a new cellular milieu which is incompatible with the pathophysiology of the disease.

A chance observation in a depressed patient of elevated serum antigammaglobulin activity (rheumatoid factor) which slowly disappeared as the depression improved, was the impetus for a large scale study of the incidence of rheumatoid factors in psychiatric patients. In collaboration with Drs. Irwin Oreskes, Harry Spiera, and Herbert Meadow, we utilized a sensitive, tanned sheep cell procedure and found that 63 percent of patients with endogenous depression had elevated rheumatoid factor titers. Schizophrenic patients as a group did not differ from normals in the incidence of elevated titers; but when depressed schizophrenics were divided from nondepressed schizophrenics, the incidence in the former group rose to 65 percent. The relationship of an autoimmunologic process to depression needs further evaluation since, if it is not an autoimmune disease per se, depressive pathophysiology may have a significant effect in exacerbating other disease processes.

Recently we have instituted an experimental clinic for the study and treatment of the child abuse syndrome. Our interest in this problem arose from a previous clinical investigation of the effects of diphenylhydantoin on a variety of psychiatric symptoms—including the breakdown in the controls of rage and violent behavior. The relationship of an altered neurophysiological substrate to these disorders is under study.

So, after a generation, the department has come full circle—except that now the radius is larger and the area of knowledge enclosed, increased by the square. The future is exciting as further insights into man's nature are revealed with all the conceptual and technological instruments his brain can create.

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Goals for the Future of American Psychiatry

ROY R. GRINKER, SR., M.D.

In Honor of a Friend

For 25 years Dr. M. Ralph Kaufman has been a leader in American psychiatry. At the same time he has been universally known as "Mo," indicating the informality and lack of pretentiousness in his relations with students, peers, and members of boards. Mo is one of the few persons well educated in basic neurology, psychiatry, and psychoanalysis. Considerably over the draft age at the outbreak of World War II, he gave up a lucrative practice and a comfortable existence to enter military service and devote his talents to prevention and instruction in the treatment of combat reactions and other problems of men under stress. As a psychiatric consultant in the Pacific Theater during the war he performed an admirable job for which he received high praise and many medals.

This experience changed his life. The sedentary and unrelieved condition of full-time private practice was relinquished for a full-time position at Mount Sinai. Those who have had continuous contact with him over the last 25 years have sung his praises in detail. I can only say from my intermittent contacts that he has been an inspiring and stimulating teacher, and a participant in local, national, and international affairs without becoming a politician in the pejorative sense. Fortunately as chairman of the Department of Psychiatry at Mount Sinai, which remained small and manageable until lately, he avoided the administrative sacrifices that cost most chairmen their scholarship and flexibility. The products of his training programs have been outstanding. Mo's development of liaison psychiatry has kept, or in many cases brought back, psychiatry into medicine.

Mo Kaufman's indefatigable spirit and widespread interests may be discerned from his curriculum vitae and extensive bibliography. Such a man, although officially forced to retire, cannot rest, but will continue his productivity. Not only does that mean further creativity for the future of psychiatry, but it also insures his longevity.

He has been an active participant in organized psychiatry—one time as vice-president, and currently as chairman of one of the councils of the American Psychiatric Association. Despite his position in the "establishment" he has been critical when criticism was justified, resistant to orthodoxy, and always concerned with the future of psychiatry—the subject of this essay.

Concern for the Future

What the future might bring and how to plan for it was not of great concern during the first quarter of this century. It was assumed that life would go on as before, that our social, economic, and natural environments would remain what they had been, that tradition could be counted on to keep our world in a steady state. It could not be imagined that what we were taught at home or in our formal systems of education would one day become less valid. Parents and teachers knew how it was and how it was going to be.

The First World War, which altered these myths, rather quickly culminated in what turned out to be only a landmark—the great depression of the thirties. Since then the acceleration of social changes has increased at a dizzying rate. The Second World War, the atomic bomb, and the myriad technological developments paved the way for several social revolutions.

Crash programs were so successful in physical engineering that attempts were made to imitate them in science, social reforms, and in "social engineering." We became conscious of what we thought needed to be done for a better future and, in the characteristic "American way," often called pragmatism, we demanded instant solutions. As a spin-off from our success in combat we declared wars against discrimination, poverty, hunger, urban decay, pollution, and even against various diseases. We were fighting so much against many deteriorating aspects of 20th-century life that we never declared war for anything.

It is as if we have been engaged in dozens of battles without knowing that each represents but a facet of the totality of what needs to be done. Our approach has been a kind of dissociated thinking without considering the interrelatedness of our goals. As a result we are threatened with defeat in all the battles against human suffering as the cost in dollars and human lives on the battlefield has caught up with us. These many battles may never be won until we apply unified thinking to the total problem considered as a system, but composed of many parts.

Even when many facets were clearly etched on the horizon we delayed action until it may now be too late. For example, the postwar population explosion was clearly foretold, yet preparation with new schools, colleges, and universities was never started. As a result educational facilities are clogged with students who are now taught in conglomerates crowded with thousands who listen only to television lectures. Hundreds if not thousands of small colleges could have been built at far less cost and would have furnished a better level of higher education.

Medical schools and hospitals fared no better. Too few hospital beds and lack of medical manpower confront us today as never before. The story is the same wherever we bother to look; where lies the fault? This is a difficult and probably useless question because only in retrospect does the problem seem to have been clear. Now we are faced with foretelling change in the future especially as we approach a new decade and soon a new century.

One of the difficulties in forecasting lies in our position in contemporary culture. We are so much a part of where and how we live, work, and play that we cannot envisage anything different. Predictions already written seem to include only more of the same with some minor variations. Certainly no Jules Verne or H. G. Wells has appeared. Either we postulate new hypothetical situations that cannot stand the test of reality or we use the guidelines of the present time. Even the members of the new discipline—the planners—seem only to recommend easier, better, or more esthetic devices to accomplish our current goals or to help us formulate them. Perhaps trend-lines can be set down and reasonable extrapolations attempted, which, mixed well with imagination, if successful will be called prescience.

Current Psychiatry

I propose to use the Second World War as the beginning of modern psychiatry (an artificial milestone to be sure) and to consider the past 25 years as current. I do this because before that time psychiatry was the "weak sister of medicine"—depreciated, limited, and static. State hospital psychiatrists who only diagnosed and classified illness were in the majority although a few American psychoanalysts were developing more progressive ideas of causation and therapy.

The war brought many young physicians in contact with people exposed to stress, and they learned some elementary aspects of psychological dynamics. The exciting discovery of the relation of emotional turmoil to physical dysfunction prompted these physicians to broaden their education in approaches that were new to this country. They had a driving need to learn more about the body-mind interaction and in the process they communicated their enthusiasm to the public who responded positively because of their own conviction of need. Some patients, aware of their neurotic difficulties, turned away from their family doctors or internists when the latter tried to insist that "there was nothing the matter with them."

At the same time the National Institutes of Mental Health, among the several founded to serve various systems of illness, underwrote a gigantic training program for the development of more manpower in psychiatry. As more and more patients sought their services, it became difficult to keep up with the need. In addition, as clinical medicine became more sophisticated and more technical, it tended to ignore the sentient aspect of the human subject. As if filling a vacuum, psychiatry stepped in to consider the person as a total being and how his life experiences contributed to the causes, course, and results of his physical illness and to his mental health, as reflected notably in difficulties in love, work, play, and in his relations to the world about him.

Perhaps an additional reason for an increased turning toward psychiatry can be ascribed to the atomic bomb, with the threat of the release of atomic energy and the complete annihilation of life on this planet. For a few years anxieties, uncertainty, and insecurities were so rampant that it seemed as if we were indeed living in an age of anxiety in which religion, tradition, and governments provided little comfort. After a few years, however, evidences of "free anxiety" decreased markedly and the quality of neuroses and psychoses lost something of their histrionic and dramatic expressions as more repressive psychic defenses were adopted. We then saw more schizotaxic personalities, more character and personality disturbances. This turning inward was associated with a greater frequency of acceptance, in fact overidealization, of psychoanalytic therapy, and at the same time with overcrowding of our decrepit state hospitals by the indigent.

More anxiety, more suffering, and greater restriction of a personal sense of freedom at a time when a greater number of psychiatrists was available made this medical specialty especially necessary. Rapidly, from its position as a tolerated field, psychiatry was given departmental status in medical schools and hospitals and became one of the five major departments in most of these institutions, prospering both financially and in prestige. What happened then could be viewed as the present status, although the term belies the rapidly changing processes in which the field participates.

Recent General Changes

Despite our innate resistance against change it is inevitable. Everything and everybody changes with variable speed. When the rate is slow we term the process evolution, when it is fast we speak of revolution. In psychiatry the Pinel-Tuke liberation of the insane from their chains is considered to be the first psychiatric revolution, while the creation of psychoanalysis is the second. Currently there is some competition among various schools of thought for the third position in the revolutionary series: psychopharmacology, community mental health, group therapy, etc. Finally there is the prediction or hope, taken from Kuhn's ideas of a scientific revolution in the physical sciences, that an entirely new paradigm may be developed.

What we have witnessed in the current era of prosperity for psychiatry is a proliferation of available facilities, personnel, and money. University departments have become vast and include university hospitals, veterans' hospitals, state hospitals, and community mental health clinics, all assembled under a single administrator called the "chairman." These conglomerates are so huge that it demands a person of considerable energy and enterprise to accept the charge of running them.

Another change is reflected by a shift from classical psychoanalysis and its derivatives to a more eclectic position by some individuals. Today there is perhaps less certainty and more doubting and questioning in regard to the explanation for a large body of empirical data. The challenges of the unknown have stimulated the curious, and although the number is still far too small, many young psychiatrists are foregoing the material advantages of private practice to become full- or part-time teachers or investigators.

Although it has long been recognized within the profession that the so-called total reconstruction of personality and the complete curability of mental illness is an ideal rarely to be achieved, the advent of psychopharmacology has justified a more optimistic view of the therapeutic potential of some individuals. Even those afflicted with the most serious psychoses and previously segregated in the back wards of the state hospitals are today being treated with at least partially effective results. There is also a greater emphasis on milieu therapy, patient participation, early discharge to the community and efforts at resocialization. The methods of therapy available for different kinds of patients have increased. Although few have been validated, an expansion of innovative procedures under various unfamiliar names represents an increased flexibility of psychiatric efforts.

Contrasted with this slow evolutionary process is the revolutionary exhortation by funding agencies, associated with threats of financial deprivation if not heeded, to devote more and more efforts to community mental health activities. The tragic aspect of this state of affairs is that while there is no doubt that the delivery of health care to the indigent in their own communties and with their cooperation is badly needed, this should not be confused with primary prevention. This "bandwagon" is not, nor can it ever be, all there is to psychiatry; furthermore, special training for community psychiatry can never dispense with the basic core curriculum required for all psychiatrists.

We are told that a "mental health center" must include five parts (no less) and that we must concern ourselves with juvenile delinquency, narcotic addiction, mental deficiency, forensic psychiatry, urban renewal, suicide prevention, etc. Unfortunately we are not magicians nor social engineers and we cannot divide by simple fission to provide the necessary manpower.

Whether this so-called revolution is a promissory note or a pious hope, we seem to be repeating the history of the 1920's when the mental hygiene movement promised everything, delivered nothing, and collapsed. Psychiatry has become extended as a field that includes all of life, but this extended field is derived from and attached to pretty shaky foundations. Perhaps we should take stock of what we know and not believe as did one psychiatrist who said that we know enough—now the question is how to apply the knowledge!

In the course of its development psychoanalysis and derivatives have moved on from a concentration on unconscious instinctual drives to become concerned with stress responses, coping devices and defenses, and other aspects of ego psychology. As it has been recognized that the functions and psychic structure of the individual in the process of maturation are derived to a great extent from experiences with people, that the major stresses of life often arise from disturbed or broken relationships with other individuals, and that the therapeutic process often prospers best in a social setting, the social sciences have become important adjuvants for the understanding of man and his problems. Thus recently these fields have fused in some areas into new hybrids—social-psychology and social-psychiatry.

Varying in complexity, social-psychiatry may include studies of the family, group, community, society, and culture. In general this field attempts to explore social systems and their effects on psychiatric processes—how the social matrix contributes to the cause, course, and results of mental illness. Contrariwise it is also the study of the effects of mental illness on social systems of various sizes.

Some promising research is being done with the family both diagnostically and therapeutically, where the emphasis is being shifted from intrapsychic processes to a group-oriented approach. In these investigations normal and disturbed families are being studied within the interpersonal rather than the intrapersonal context, and families are being studied as "systems" rather than as a conglomeration of individuals.

Group studies have been conducted in therapeutic settings, but group therapy is a vague and poorly defined though ubiquitous term applied to any process observable in groups. Only lately have the principles of small-group dynamics been explored.

Community psychiatry is a relatively new venture rather suddenly crystallized by the increased permeability in hospitals, clinics, and halfway houses, and the merging of community aspects of rehabilitation. It lacks both theory and operational methods. Even communities are poorly defined, namely, as "clusters" of people having "common destiny." Community psychiatry deals with a wide variety of relationships among community social agencies, resources, clinics, and hospitals. It includes a wide variety of personnel concerned with administrative, therapeutic and research functions. There is no specific discipline and certainly no community psychiatrist knowledgeable enough to encompass the whole sector which includes a broad network of agencies. At present community psychiatry is largely an organizational concept.

Since psychiatric phenomena are social, to the extent that they arise from a social matrix; since they are precipitated, flourish, or decline under various social conditions, that is, they have an "epidemiology;" and since therapy depends to a degree on social and cultural factors, our interest in the contributions of the social sciences to the problem of etiology, although late and naive, is now growing. If we ever have anything to contribute to prevention, it will be through widespread social education at all levels. If our therapeutic efforts are not to be limited to the few, there will have to be an increased interest in methods of understanding and eventually of treating the many, based on, but not simply a direct extension of, our understanding of the individual. For these purposes education of psychiatrists will require extensive broadening, if not to widen the extent of their functions, at least to facilitate the cooperation of psychiatry with psychology, sociology, and anthropology.

If we look at the vast area which psychiatry now covers without even being able to guess how much further it will extend, since psychiatry seems to be as broad as life itself, we find divisions that are based on a number of points of view or orientations. We can recognize easily the orientation of age which divides psychiatry into that concerned with children, adolescents, young adults, adults, and the aging. Some frames of reference are problem-oriented such as disease classifications, behavioral manifestations, and dynamic or psychoanalytic concepts. These are approaches which deal with specific problems from separate frames of reference. There is then the action-oriented psychiatry which is concerned with the study of epidemiology and "social engineering," which has as its prime aim that of changing society and as its conviction the belief that as a result its people will no longer suffer from those frustrations and conflicts that end in sickness. Finally, there is an approach-oriented conception which can be subdivided into the biological, psychological, and the social. Sometimes these are linked together in one biopsychosocial approach and hopefully one day, into a general system.

Is Psychiatry a Medical Specialty? Is It a Science?

Here we are faced with the problem of definition. To the extent that psychiatry, like other branches of medicine, is a body of knowledge concerned with the diagnosis, treatment, and prevention of a delimited catalogue of human disorders, and that like other specialists, psychiatrists are clinicians who strive to make sick people well, psychiatry surely ranks as a medical specialty. Unfortunately the problem is not so simple, for in some hands at least methodologically the practice of psychiatry is far removed from the criteria of a scientific discipline. Some practitioners, for example, appear to disdain the need for precise diagnoses or classification and exhibit a minimal interest in the validation of their results, while adhering dogmatically to their unvarying techniques as if the latter constituted an article of faith rather than a scientific exercise.

At the other end of the spectrum are those who assert that mental illness is a myth and worse yet, that those who have been hospitalized for their deviant behavior are victims of a conspiracy. Others, while admitting the reality of mental illness assert that it is the product of faulty education and can be corrected by re-education. To the degree that the latter is at best a poorly defined entity the field has been inundated by an array of persons who, possessing minimal or no qualifications for the job, have boldly entered the field as so-called therapists.

Clearly the questions posed at the outset of this section cannot be answered with a simple yes or no. It has long been established that it is not the subject matter which determines whether a given undertaking is a science, but rather the method or system by which that subject is approached. The stars in the heavens are of equal interest both to astonomers and astrologers, but methodologically these two are several light years apart. By the same token we would assert that under appropriate methodological auspices psychiatry is a science that ranks with any other medical specialty. Yet we would go even further and claim that in view of the vast area it seeks to encompass it transcends the limits of a medical specialty and should be viewed as a multi-disciplinary field devoted to understanding processes within all organismic levels and all human objects, social groups, and material aspects of the outside environment.

Psychiatric Therapies

Recent advances have improved the outlook for many persons afflicted with psychiatric disorders both within the confines of mental hospitals and without. In a later section I shall discuss the components of scientific psychiatry as parts of a total system. Specific therapies may be directed to any part that may be functioning defectively and thereby affecting the whole. Even biogenetic disorders giving rise to enzymatic, endocrine, or metabolic disturbances may one day be treated by appropriate substitutions or antidotes. The range of therapies applicable to disorders of mentation or behavior is indeed wide, and, sooner than we believe, it may become even more extensive. Aside from the use of electroshock or drugs, therapy for the vast biopsychosocial system has largely concentrated on the psychological component. Even here therapies have spread from classical psychoanalysis to psychotherapy of individuals, marital pairs, families, and groups. The social component moreover is being approached by behavior therapy, milieu therapies of various kinds, and attempts at resocialization and work rehabilitation. All of these require appropriate techniques which are still in a preliminary stage of formulation. One of the most vexing problems encountered in any form of psychotherapy is an adequate system for evaluating results. Enthusiasm for particular therapies has far outrun the validation of results, giving rise to such unanswered questions as: who treats what kind of patient, with what kind of trouble, in what kind of setting, by what methods, with what results, as measured by what criteria? Hardly a single "what" is known today!

Another problem concerns the limitation of trained personnel in the field. Today the demand for help is so great that, despite the geometrical increase in mental health professionals derived from greatly expanded training facilities, we are still woefully short of manpower. The gap between demand and capacity is increasing so that we need to employ ancillary subprofessional helpers to serve some functions that the professionals cannot undertake alone, but can only supervise. This is a delicate matter and requires a great deal of thought and practical testing.

People approach us for a variety of reasons few of which require more than focal exposures and segmental approaches. Most difficult and arduous are those problems that are internal—manifested by depression, dissociation, repression, and a wide variety of characterological and personality deformation. Such disorders of mentation need longer therapies in depth.

Others manifest crises-reactions to unusual situational problems. They are often quickly rehabilitated and returned to their previous stability if properly treated. Some have more chronic and disabling problems in coping with more general stresses. Still others are considered in need of help by those who observe their aberrant behaviors in social or interpersonal situations. The point is that there are many kinds of problems independent of formal diagnoses. For all these troubles, from total disorganization and inadequacies in thinking and behavior to partial or temporary dysfunctions, there are applicable methods of therapy. Our job is to know what is appropriately effective for rich or poor, schizoid or hysterical.

Whereas our goal is clearly to help people become more "healthy" or "normal," relatively recently psychiatrists have tended to ignore the vexing question of what is healthy in any given society. Today psychiatrists are beginning to study normality not as an absolute concept but as a system depending on that society and subculture which furnishes the matrix in which the subject develops and exists. In a sense psychiatry and sociology are approaching each other in this area.

It is clear that the word 'coping' is becoming more popular; in fact, it serves as a neutral and unifying symbol for many disciplines, since 'adaptation' is biologically oriented, 'defense' has psychodynamic connotations and 'health' and 'normality' are bogged down with judgmental values. The behavioral sciences may be united under the banner of 'coping,' studied with reference to its effectiveness at various times and places and subject to improvement by a variety of therapies.

The health-illness systems cannot be separated to define health and illness each in absolute terms. Health is dependent on several factors, such as age, cultural and social attitudes, internal compensations, defenses, coping ability, etc. In general, health is maintained when strains affecting one part of the biopsychological system are compensated or counteracted by other parts. Even a new relationship or equilibrium of the parts caused by stress may eventuate in a health adaptation.

In general, the health-illness system involving body and mind extends from genetic to sociocultural factors and encompasses development and decline. This includes birth, infancy, childhood, adolescence, young adulthood, maturity, aging, and dying and death. Each phase has its characteristic internal processes, its specific stresses, and its capacities for defense, for coping, and for reconstitution. Each and the whole have their interfaces with specific sociocultural environments—their "eco systems." This concept transcends departmental or disciplinary lines, and it combines knowledge of laboratory procedures, life in pairs, families, groups and the larger society. It is concerned with phases of stability, stress-responses, and despair.

Each phase has its appropriate variety of therapies chosen from the wide range now in existence, including crisis and emergency brief therapy for persons coming directly from the community, or as a back-up for community mental health centers. My own experience suggests that there seems to be an unnecessary dichotomy between individual dynamic psychotherapy and milieu or social therapy. We need to develop a respectable eclectic viewpoint, abandoning nothing save dogmatic preconceptions, and putting such technique in its proper perspective to the end that the main objective should concern the particular therapeutic needs of each disturbed or deviant person.

The Science of Psychiatry

From the foregoing it is evident that psychiatry encompasses far more than the matter of therapy and that as a scientific entity it admits a wide variety of definitions. While some consider it an applied medical science, others view it as part of the behavioral sciences. Another group would limit its scientific property to its biological roots. Despite its proven uselessness and futility, the ideological struggle implicit in the foregoing points of view persists and is emphasized by the diversity of psychiatric societies, and by the multiplicity of theories concerning therapy. A more rational approach is to consider scientific psychiatry as a total field or conglomerate composed of many parts or contributing sciences. It is not necessary here to enumerate them; they extend from biogenetics to sociology and include contributions from all disciplines concerned with the study of behaviors of man in health and illness. Here behavior is considered broadly in the sense that biochemistry, endocrinology or physiology may be viewed as special manifestations of behavior much as is man's conduct in society. The inclusion of all these behaviors is the ultimate admission of psychosomatic unity. The total field needs a name, and, awkward though it may be, "biopsychosocial science" conveys the breadth and comprehensiveness of the approach, while avoiding unsatisfactory polarizations. It also clearly indicates the multidisciplinary nature of this life science whose advances depend on progress in its component part-sciences.

A psychiatrist realizes that a sophisticated mode of thinking views behavior as a conglomerate of allocated functions designated and studied by several disciplines. Scientific psychiatrists, as contrasted with ill-trained or untrained therapists, try to put all these together in a meaningful relationship or organization, striving toward establishing a unitary theory. As L. L. Whyte stated, our aim should be the search for "unity in diversity and for continuity in change" which emphasizes one general form beneath all dualisms.

Control and regulation in open living systems are achieved by means of communication, transmitting information within feedback arrangements, but involving many complicated reverberatory cycles rather than simple linear chains. The living organism not only reacts to its environment, but it also actively searches for changing goals by means of which it differentiates, grows, learns, and evolves. This proposition contradicts the robot model of man who supposedly searches for needs, seeks relaxation of tension from his social environment, and thereby achieves homeostasis. There is more to life than maintenance and survival. In fact, the human capacity for symbolic representation functions as a powerful force for change apart from biological evolution. New symbols are transmitted to other generations by means of language. Thus, symbols are the genes of culture.

Our essential difficulty includes our habitual two-dimensional imagery. What is required is a three-dimensional spatial perception plus a recognition of temporal dimensions. Because this is so difficult I have proposed an integrated model for the kind of imagery necessary. This is a transactional model that encompasses process and relationship.

The model would assume the form of a cylinder open at both ends. Height represents levels of complexity. At the bottom, extension could occur to the physical world, the top to the infinite cosmos. The inner-outer depth of the cylinder represents the dimension of differentiation so that the center is least differentiated and the surface is the point of maximal differentiation equated with growth and decay or at least change in the life cycle.

On the surface of the cylinder would be three columns: One represents somatic variables such as physiological, biochemical, enzymatic, cardiovascular control, nervous system, drives, and their regulatory and control systems; two represents the psychological variables such as memory, perception, cognition, motor behavior, and their controls; and three represents environmental factors that surround the organism, stimulating growth and creating stresses and strains. These three columns also represent the traditional subsystems of the field designated as somatopsychosocial.

The model does not assume causal relationships between and within columns, but assumes that a functional relationship does exist among and within the columns in any direction giving rise to an infinite number of contingent variations depending both on heredity and experience, and permitting individual and patterned behaviors with specific meanings.

The relationships among the parts or subsystems occur at their interfaces in a reverberating cyclic manner, each acting on the other. Such transactions can only be observed among two or three variables, keeping the others in mind and holding them reasonably steady at one particular point in time.

The model permits us to move in several directions: from trait to trait or across systems, as well as across time in one system, permitting a longitudinal study of the changing nature of specific functions over time. It must be recognized that the designated systems are concepts whose relationships are descriptive and not explanatory. Subsequent explanations and attribution of cause or purpose in adaptation constitute a justifiable teleology, based, however, on inferences. These are then hypotheses to be tested by means of appropriate designs applied to health-illness systems which cannot be fractured into health and/or illness.

The cylindrical model which is based on General Systems Theory adds several dimensions. For example one cannot rely only on the principle of isomorphism indicating general laws or regulation applicable to all subsystems. Each has its own evolutionary developed differentiated functions. The model permits an approach to development or differentiation and regression or redifferentiation within age-specific critical periods after which and beyond which movement or change is unlikely. A system has a past which is the developmental history of its parts. It has a present as its characteristic form or style of integration. And it has a future in its functional relationship with other systems at their interfaces. Within the system and between systems communications are reverberatory or cyclic, what we term transactional. Furthermore, just as all parts function or behave, so the process involved in transactions carries information controlled and regulated by systems of feedback. Whether through energy exchange, chemical substances, words, gestures, or more gross behavior, the important common principle or isomorphism in all systems and their parts is the communication of information as a transactional process at a particular time in a particular setting.

It is not my purpose to discuss specific areas of needed research nor areas of investigation that seem more fruitful since these are time- and culture-bound. Instead, I am concerned with several principles, one of which needs emphasizing at this time. It is a restatement of the major questions applied to problems of the health-illness cycle; *what*, *how*, and *why*? Especially, because so many disciplines are working in more or less isolation on segments of human functioning in various disturbance, it is important to know if everyone is working on the same "what," or the same behavior or mental disturbance. Diagnosis, classification and categories are basic to integration of findings achieved by many techniques. The "how" of etiology and the "why" of adaptational significance would be lost unless the same condition is observed by all.

Teaching Psychiatry

For what ultimate functions do we teach our students, whether they be residents or fellows of various disciplines? The recent Coggeshall report for the American Association of Medical Colleges omits entirely considerations of quality. It states that there is an increasing need for doctors, therefore more students should be accepted, early specialization encouraged, and the curriculum shortened. It is a short step from this to set up special schools for the education of general practitioners; the counterpart would be to train residents to become state hospital or community psychiatrists. Accepting second-class residents would guarantee the graduation of second-class psychiatrists who as staff members of our institutions would maintain the universally low standards of care. Improved input of our training programs and the desired output into our state hospitals requires an entirely different strategy. Neither the training nor recruitment of competent psychiatrists can be improved until conditions in our institutions are changed. By this I do not mean better fiscal management, although this has been bad enough. I mean that what we need is competent enlightened professional leadership that can change the working environment to something more conducive to a stimulating career and the opportunity for self-development. Then our graduates may choose to work for the state, especially since all private practice probably will soon be financed by governments.

The greatest danger is an attempt to orient a training program toward a predetermined direction for graduates. There can be no one goal for trainees, all of whom should be taught the fundamentals of general psychiatry with options for special studies during their final year, but a core curriculum is essential for all future psychiatrists. They should be exposed to a variety of excellent models who function as good directors of education and as good supervisors within an environment containing stimulating clinical research.

What are the training centers doing about experimenting with education for psychiatrists? There is little deviation in opinions by the directors of individual centers because in truth we are all now teaching pretty much alike and with practically the same content.

The powerful focus in shaping our educational program has been the students. Inquiry today should be directed toward those influences that encourage students to accept a specific theory and its methods and to reject another. Hopefully modifiable are the general intellectual values to which the intelligent student is exposed during his premedical and medical education and his internship. It is during his premedical and medical education that he develops identifications with various models and incorporates the ideals of those teachers significant for his future professional career. If clinical psychiatry is taught as a specialty independent of other clinical disciplines and the basic sciences, the model that the student incorporates will become highly restricted and "premature intellectual closure" may occur. However, if residency training gives an opportunity for the student to be exposed to all of the sciences contributory to psychiatry, and his experience in therapy involves the exposure to many methods, none of which is presented in a spirit of dogmatism, the student may develop or keep an open mind. It should be recognized, however, that in some students the adoption of a relatively dogmatic point of view and its resultant premature closure may be less the consequence of external influence than the answer to a distinct individual need, specifially the matter of emotional security, which depends not infrequently on a sense of intellectual certainty. Such issues aside, ideally, it is hoped that students can avail themselves of a wide spectrum of influences, embracing both the interest of the psychoanalytically-oriented supervisor in unconscious mechanisms, dreams, and transference-countertransference phenomena and the essentially practical and common-sense viewpoints of the more pragmatic therapist, thereby providing them with the best of all possible academic worlds.

This leads me to the point where I think opportunities for minimizing the premature closure of the future psychiatrist may be. It is in the medical schools and their premedical affiliations where the appropriate model of the general psychiatrist should be instituted. This means that clinical psychiatry should not be taught independent of other disciplines but rather within the matrix of the basic sciences and the clinical specialties. Only in this way can the student gain a proper perspective of the role of psychiatry and an early and abiding realization of the pervasive importance of the human aspect of medical practice and of the complex interaction between the mind of man and problems of health and disease. Hence the professors of psychiatry, well before the internship and the residency, have an opportunity of creating models which correspond to what we believe general pychiatry should be. Teaching psychiatry is a difficult task at best. It is not as in other disciplines a process continuous from medical school through the internship, residency and medical or psychiatric practice. It is in fact often a discontinuous process because in some institutions its various segments have remained unchanged for many decades. Hence the decision of many medical students to enter the field of psychiatry may be determined by the quality of the teaching. There is no doubt, moreover, that the liaison psychiatrists often supplement the educational process by teaching on the general wards. First year residents in psychiatry enter a strange world without prior introduction and suffer the anxieties and depressions so well known in every training center. Any decision to abolish the internship will necessitate changes in the medical school curricula which may not be readily achieved by those faculties that have been characterized by persistent inertia.

It is a pity, moreover, that medical students are not prepared with adequate exposure to biology as, for example, human genetics, nor to sociology and anthropology. Modifying the curriculum in medical schools to include more electives promises improvement, but only if the electives are improved in form and content. More multidisciplinary methods of teaching could help the student extrapolate from the findings of the experimental science to the problems of man. Greater emphasis on observations of behavior to complement inferences about mentation could introduce a unitary system of thinking.

Epicrises

American psychiatry has become a large organizational structure recently subdivided into several councils, each one of which delegates committees and/or task forces to consider special problems within a designated time limit. As a result the extent of the total field is increasing in geometrical proportions. Its parts have each been developed by highly specialized and interested persons who pursue their goals as if they represented all of psychiatry. Because control, regulation, and integration of this system are not adequate I have likened it to a person riding a horse in all directions. But worse than this, each segment insists on occupying a significant place in the training curriculum. Testing and evaluation of pilot studies of these new enterprises are woefully lacking; ideas have been assumed to have immediate operational efficacy.

Like any other medical specialty, psychiatry functions to furnish treatment, to teach, and to investigate. We blithely continue to treat without substantial knowledge of our results and engage in bitter verbal battles with those who treat differently. Even an eclectic position is attacked. We teach increasingly immature students with surprising authority in light of our limited knowledge.

It is tempting to combine all the possible answers to the questions regarding future goals in psychiatry by a succinct statement: "Do the best for the most." But that is much too simple and simply avoids all the substantive and organizational issues. I do not believe that the future, as far as I can see, will be characterized by a scientific revolution producing a new paradigm; nor do I believe that the present system of psychiatry will be destroyed. Change, modifications, and implementation will occur, and in some areas considerable progress will be made. It is important, however, if progress is to be made, that we maintain both a continuing evaluation of the field and of ourselves and skeptical, doubting, and questioning attitudes.

Care of patients is our primary medical responsibility. Despite the common overenthusiasm over new methods which hopefully would empty psychiatric hospitals, they are destined to remain in existence. Methods will improve to prevent the permanent regression of some patients and to rehabilitate those who have abandoned all hope, especially in the state mental hospitals. Short-term hospital stays oriented to temporary failures in coping and emergency care of critical responses are beginning to prove highly effective.

It is becoming more evident that an understanding of the susceptibilities to and the recovery from characteristic stresses are different in various phases of the life cycle. Hence specialization into age categories is increasing. Inpatient management of peer groups show promise of greater effectiveness.

Community clinics may improve the delivery of services but the returns from this experiment are not yet in. Until socioeconomic environments are altered through political and other reforms, primary prevention is still a pious hope. I am convinced that as research in psychopharmacology becomes more effective symptomatic therapies with specific drugs will become more effective and widespread.

Research in psychiatry is a prime goal for its future. For this more than lip service is required. The part-sciences, especially biogenetics, epidemiology, and neurochemistry, have grown rapidly, and in some respects have outpaced clinical psychiatry. Lacking are young and dedicated clinical investigators, models for their emulation and funds for their initial support.

The extent of the field needs to be defined, for at present it is expanding theoretically to infinity. We should be more aware of the composition of the component disciplines in the field of psychiatry. More important is the development of principles of organization of the parts into a longer whole maintaining a level of integration. The General Systems and the Transactional Models are beginning to take hold for this issue, to reverse the present state of scientific polarization.

The approaches to human problems may take a variety of forms: age-oriented, problem-oriented, action-oriented and approach-oriented. But each needs a definition of "what" is being considered. Diagnostic and nosological classification is woefully poor and must precede the development of answers to questions of etiology and purpose.

Without listing the vast areas of ignorance requiring much research some foci demand urgent attention. Among those are a broader approach to psychophysiology and response-specificity, the phases and types of health or normality, and a better delineation of stress-coping devices.

There is some hope that the study of evoked potentials and other electroencephalographic (EEG) phenomena will develop some discriminatory analyses of behavioral functions. The immunological aspects of disease may be applied to certain disturbances in the central nervous system which may be due to autoimmunity phenomena. Certainly, the studies of sleep, dreams, and hypnosis may contribute much to the phenomena of normal and aberrant kinds of thinking and behavior. Finally, I think there is a great deal yet to be done in the study of biogenetics and in child development, although this is still in its early phases. We need to know more about the development of normality in children, adolescents, and adults, and about the adaptations under various conditions derived from ego functions, particularly in their coping devices.

The variety of these dimensions often has expressed itself in a conflict of either or. Sometimes this is resolved by the adoption of a reductionistic frame of reference and sometimes by a humanistic frame of reference; such polarities are often considered quite separate. On the other hand, some attempt to resolve conflicts of this nature may be achieved by the development of general or unified theories of which General Systems Theory is one example and transactionalism another. These global theories, however, are not operational and often serve as escape hatches. The umbrella of a general theory only encompasses other less global and smaller theories, each one of which may contribute to hypotheses which require well designed operational research.

Education in psychiatry is a multileveled enterprise from medical school throughout the specialist's life. There are no "instant" specialists or subspecialists; a basic core curriculum is mandatory for all. Interpolation into many fields is then feasible but there are no short cuts to efficiency.

Coinciding with the widening dimensions of the field, adequate residency training in three years is becoming almost impossible. It may be necessary to extend the time or to create special centers for specific education in parts of psychiatry.

No one has the capacity to teach every phase of psychiatry; we need more specialists who can also serve as models for the students. To become a good teacher is difficult. He needs observation of others, experience, and critical instruction himself. There is a mix of courses, seminars, conferences, and clinical experience in the curriculum which each institution must find for itself.

Furthermore we cannot expect the graduate to fulfill all the functions of psychiatry even in therapy. What he learns from several diverse models of his teachers and supervisors must be synthesized and added to his template or personality or life style. In some activities he will do better, in others, the same or worse. His job is to discover what he can do best and to pursue this function to the limits of his capacity.

Organization problems in psychiatry are becoming more difficult with a geometric increase in paper work that threatens to inundate us. Our financial support is rapidly drying up at the same time. There is a growing tendency to commercialize the support of psychiatry, replacing basic research support with the dramatic community mental health bandwagons and by what the granting agencies believe will result in rapid payoffs.

There is a pressing need for crucial breakup of the psychiatric conglomerates, which are impossible to manage, into smaller departments with scholarly and scientific chairmen who can serve as adequate models for serious students. True, there is a manpower shortage for all that psychiatry is supposed to do, but the assumption of professional values and the abnegation of political points of view and pressures is a future necessity.

A better relationship among the other mental health disciplines—clinical psychologists, psychiatric social workers, and nurses—may improve the distribution of services. Subprofessionals and indigenous aides when properly trained and directed may be of great assistance. All this bespeaks the need for an improvement of an organization principle which is applicable to all systems—what Weiss calls "order in the gross with freedom in the small."

Psychiatry's system of study has become greatly extended to include many parts from biogenetics to culture, and has exposed many interfaces with other systems, from education to world organization. We therefore have the responsibility for leadership. This requires abandonment of ideologies and a search instead for an approach to systems and the properties and functions of organizational processes. In 1963 in the second edition of our book *Men Under Stress*, Dr. Spiegel and I wrote about what has been and is slowly happening in psychiatry.

"Ego psychology has brought psychoanalytic theory and method into a somewhat uneasy commerce with experimental and social psychology, on one side, and with ethology and physiology, on the other. Sociology and cultural anthropology have made many contributions to our understanding of the environmental variables correlated with mental illness. Group dynamics has developed rigorous methods for determining the structure and function of group processes in a variety of circumstances. Studies of family behavior and its impact upon the individual, in sickness and in health, have thrown light upon the development of the ego and its characteristic modes of defense. Interdisciplinary methods of collaboration have vastly enlarged the techniques available for determining the sources of psychopathology in the community and in various national groups. Throughout all this bubbling research activity and melting away of traditional scientific boundaries there runs the theme of a constantly broadening therapy. Personality disturbance—whether mild or severe—is currently approached through biological, psychological, and social strategies, either separately or in combination with each other, in the effort to relieve the stress upon the conflict-resolving mechanisms of the ego."

This statement is valid today and in my opinion represents the future goals of psychiatry.

East Harlem: An Initial View

MARX BOWENS, M.S.W.*, MARGARET C. OLENDZKI, PH.D.,
CARTER L. MARSHALL, M.D., COURTNEY B. WOOD, M.D.,
AND CHARLES H. GOODRICH, M.D.

East Harlem is one of New York City's historic and most distinctive communities. In the past, when the railroad was the major means of transportation, passengers from all over the country saw East Harlem as their first view of New York City—the tenements, drying clothes flying on lines strung from the tall poles, women with their elbows on pillows as they leaned from the windows looking down upon the congested streets below—from the New York, New Haven and Hartford Railroad speeding over the bridge at 138th Street. Today, as the Penn Central trains rush from the tunnel at 97th Street, the escaping commuter is provided with his last look and a reminder of the dirt, noise, and conflict of "the City." Although the view and many of the old tenements still remain, they are gradually being replaced by the tall public housing developments, the "projects."

Boundaries and Topography

East Harlem is located in the northeastern corner of Manhattan along the East River. The generally accepted boundaries are Fifth Avenue to the west, 96th Street to the south, and the Harlem River to the north, while the East River (including Randall's and Ward's Islands) forms the eastern boundary. The heart of East Harlem lies between East 96th and East 125th Streets.

This whole area, including the triangle above 125th Street, has been designated as Community Planning District Number 11 by the City Planning Commission (1). Geographically, then, East Harlem is a distinct community with its boundaries—historic, natural, and man-made—now reinforced by the City's official designation of the area as a separate Community Planning District. (It is one of 12 such districts in Manhattan; one of 62 in the entire city.)

This area, the original Indian name for which means "Flatlands," is generally level. The land does rise between Madison and Park Avenues, with the principal elevations at Mount Morris Park, at Duffy's Hill (Lexington Avenue and East 102nd Street) and Carnegie Hill (Park Avenue and East 97th Street). These elevations, and the slopes along many of the east-west streets, provide a commanding view of the East River, The Bronx, and midtown Manhattan.

Developmental History

East Harlem, known as Muscoota to the Indians and as Nieuw Haarlem to the Dutch, was first settled by Europeans in 1636. Until the middle of the nineteenth century, the area consisted mainly of farms tilled by the Dutch,

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* This descriptive paper is based upon a report: "East Harlem: Basic Background Information," prepared by Marx G. Bowens for The Mount Sinai Hospital, September, 1969.

English, and German migrants (Franklin D. Roosevelt's grandfather was one of them). There was a small trading center for the agricultural district along the shore, about the present location of East 105th Street.

Transportation has had a major influence on the development of the urban community as well as on the various sub-areas within the city. The opening of the New York and Harlem Railroad in 1837 was the first step in linking East Harlem with the rest of the city. The horsecar railroad was soon followed by a steam-railroad line and, in 1880, by the elevated line. This link provided the impetus for the development of East Harlem to accommodate the surging European immigration of the 1890's. The more historic or traditional lower-Manhattan tenement areas had become completely built up; land costs skyrocketed. The railroad opened up cheap land areas and provided an extension of the long, north-south arteries to the Harlem River on the north. A speculative building boom of a solid and dense grid of Old and New Law tenements followed. This type of physical development of the area was virtually uninterruted by either park or open space, in order to permit maximum exploitation of the land.

The emergence of the railroad tracks from Carnegie Hill over the Harlem flats thwarted the northward continuation of the luxury residential housing which had begun to characterize lower Fifth and Park Avenues. Consequently, East Harlem was laid out as a low-income area isolated from the rest of Manhattan by the railroad, by Central Park, and by the industry which grew up along the rivers. Those parks and open spaces which did exist were restricted to the periphery of the area and served as natural barriers separating East Harlem from adjacent communities. They did not interrupt the stark and unrelieved street system of East Harlem itself nor provide much-needed recreational space in the heart of this congested community.

Central Park, acquired in 1856, forms a fourteen-block section of East Harlem's western boundary. However, the Park's influence as a recreational resource has not been felt strongly by the residents of the area. Direct access to Central Park has been prevented by the barrier formed by solid blocks of city- or regional-oriented institutions which face the Park and extend along most of this boundary. In addition to The Mount Sinai Hospital and Medical School, these institutions include the New York Medical College-Flower Fifth Avenue Hospital complex, the New York Academy of Medicine, the Museum of the City of New York, the Department of Social Services' Children's Shelter, and the Home and Hospital for the Daughters of Israel; when large luxury apartments and a middle-income cooperative are included in this buffer, it extends from East 96th Street to East 109th Street (2).

Four phases in East Harlem's development may be distinguished: its original build-up of population from the 1890's through the first World War; the period between the wars when Negroes and Puerto Ricans began to replace the earlier immigrants; the rapid increase in public housing in the forties and fifties; and a new phase towards diversity beginning in the sixties.

Initial Phase

During the 1890's, successive waves of Irish, German, Jewish, and Italian immigrants moved into East Harlem. The Irish were the first residents in East Harlem, with Jews and Italians soon arriving in increasing numbers. Many of the Jews moved to East Harlem from the Fourth and Sixth Wards around Park Row and Baxter Street and from the Lower East Side. Italian immigrants came in such numbers that by the First World War East Harlem became New York's "piccola Italia," the largest settlement of Italians outside Italy itself.

Although the Jews and Italians became the dominant groups, East Harlem actually consisted of a wide variety of peoples of diverse national origins. Many old-timers often mention that East Harlem was a "replica of the map of Europe." For example, the Greek Orthodox Church of St. George and St. Demetrios at Lexington Avenue and East 103rd Street was the center of a small Greek settlement. A block west, there still stands the vacant and recently charred remains of Yeshiveth Torath Chaim School of Harlem which was organized at the turn of the century and built in 1914.

The Italians originated mainly in Southern Italy and Sicily. Most of these "newcomers" were peasants without skills and they entered the labor market at its lowest level. Some of the Jews were unskilled also, but many (together with some Italians) had skills in trade, or were peddlers of ice, fruit, vegetables, clothing, dry goods, and junk. Some opened shops and developed thriving businesses. Others went into independent service trades, becoming barbers, tailors, and shoemakers. Development of rudimentary or limited skills provided the means of entry into the expanding garment and construction industries.

Second Phase

By the 1920's, the upwardly mobile Jewish residents had already started to move out to the other boroughs of the city and to the suburbs. The Italian population also gradually diminished with the improvement in economic status and the "Americanization" of the second- and third-generation Italians.

In the late twenties and early thirties the vacuum in the housing stock—Old and New Law tenements mostly over sixty years old and changed very little since the turn of the century—began to be filled by Negroes and then by Puerto Ricans. The early growth of the Negro population, spilling over from Central Harlem and increasing simultaneously in both The Bronx and Brooklyn, was quickly outstripped by the Puerto Ricans, the newest "newcomers." There were some 500 persons of Puerto Rican birth in New York in 1910; 7,000 in 1920; 45,000 in 1930 (3). By 1940, the predominant concentration was in East Harlem, El Barrio. Part of "Little Italy" became "Spanish Harlem" and, like the Italian settlement before it, became "the largest settlement of Puerto Ricans outside Puerto Rico."

The lack of language, education, or job skills that often characterize the newcomers to a country or a city were less of an obstacle to the Jewish and

Italian immigrants than to their later Negro and Puerto Rican counterparts. The former, unlike the latter, were supported by strong familial, neighborhood, religious, communal, and philanthropic institutions. The Irish, Jewish, and Italian migrants came to an open and expanding economy with an almost limitless capacity to absorb relatively unskilled labor. By the time the Negroes and Puerto Ricans reached New York City in large numbers, the willingness to work was no longer sufficient requisite for success in "the land of opportunity." The willingness to "push a wheelbarrow" (now seldom seen) was no longer the first step to move up in the construction industry; the sweat shops or long hours of sewing at home could no longer serve as the bottom rung of the garment industry.

The early absence of voluntary associations, notably among the Puerto Ricans, meant that governmental aid was needed to facilitate the adjustment of the new cultural group; this need was first recognized by the establishment in 1930 of the New York office of the Department of Labor, Migration Division, Puerto Rico. Various City departments (for example, the Committee of Inter-Group Relations, the forerunner of the present Commission on Human Rights) also provided many special services for the Puerto Rican migrant over the past thirty years. More recently, the Puerto Rican community itself has recognized this need by building upon the myriad hometown or social clubs (fraternidades) and developing a number of city-wide Puerto Rican organizations (for example, Aspira, the Puerto Rican Community Development Project, and the Puerto Rican Forum).

Third Phase

The forties and fifties might be considered as a third phase of East Harlem's development. The shortage of housing and the age and deteriorated condition of the available housing stock, coupled with the low income of its residents, required public intervention. The major action taken by the city was the provision of public housing. The first public housing project, East River Houses, was completed in 1941; twelve more followed in the seventeen-year period between 1948 and 1965. This action recast and case-hardened the mold of East Harlem as a low-income area. Such a development was resented by the Italian community and provided the basis of the initial tension between the majority and minority communities. This public housing activity, more extensive than that in any other part of the city, gives the East Harlem community much of its present character and provides the parameters of many present problems: physical, economic, and social.

Fourth Phase

During the sixties, East Harlem may be seen as entering its next developmental phase. Community resistance to more low-income public housing crystallized, and was actually fused into effective action in the case of Franklin Plaza (4). The city planned to turn the blocks between 106th and 108th Streets, from

First Avenue to Third Avenue, into yet another low-income project. But the community felt that this trend toward more and more public housing should be arrested, indeed reversed. It was strongly felt that East Harlem, if it was to retain its vitality, must not become an economic, nor an ethnic, "ghetto." And so, in 1962 it was finally agreed that Franklin Plaza should be developed as a middle-income cooperative.

Riverhead, at the upper end of Fifth Avenue, completed in 1968, was also built as a middle-income cooperative.

During this period since 1960, there has been increasing interest and action by the private sector. When the city, which owned and operated the old Park Avenue Market, was about to close it down and dispossess the tenants, the latter were able to establish their own successful cooperative. A number of local organizations in the southeast part of East Harlem combined to form the Metro North Association (5) and, starting as a local housing violation campaign, a "bootstrap" operation, it began to evolve with the city a local rehabilitation program and a renewal plan for this sub-area (6).

It is true that the formation of Metro North was made possible by new federal aids and tools such as the federal housing legislation; but this development signaled a change in the role of the local community in the planning process. The principle of community participation had been enunciated some sixteen years earlier in the Housing Act of 1949. But in the ensuing years, the philosophy and the attitude of the old Slum Clearance Committee lingered on. When Metro North emerged, however, this local area, aided by a Chicago-based foundation, became an active participant in the planning and implementation process.

The Italian residents, in owner-occupied buildings, undertook the rehabilitation and renovation of their property privately. New federal aids have recently broken the bank moratorium on assistance to property owners in the area, a moratorium which had coincided with the influx of Negroes and Puerto Ricans in the thirties. More recently, other private institutions have displayed interest in the East Harlem community.

Various programs are presently being planned for the East Harlem area. Harlem-East Harlem has been designated as a Model Cities Neighborhood; the area includes most of East Harlem down to 106th Street (but excluding the section north of 127th Street between 5th Avenue and Park Avenue) and it also extends into Central Harlem as far as Morningside Avenue.

The following Model Cities programs will affect parts of East Harlem:

a) Milbank Frawley Circle, a plan to renovate the area to the northeast of Central Park.

b) East River Urban Renewal, a project sponsored by Local 1199 which will house about 1,350 families. Educational, social, and other community service facilities will be provided for both tenants and local residents. Mount Sinai has been invited to develop the health care services.

c) East Harlem Triangle, a proposal to redevelop this area for mixed residential and industrial uses.

d) 125th Street Zoning and Transportation Study is in the early stages of considering crosstown and other traffic pattern changes.

e) Penn Central North is in an even earlier stage of studying possible development of housing and air rights over the Penn Central tracks north of East 96th Street.

Metro North is located south of the Model Cities Neighborhood. Several projects in the southeast corner of East Harlem go by the name of "Metro North"; e.g., a public housing site and a neighborhood development program. Plans for the area include middle income housing and the expansion of Metropolitan Hospital.

Administrative and Service Districts

Although the Community Planning Districts have official status in New York City now, each of the various city departments and agencies still has its own administrative boundaries. East Harlem falls into at least two, and sometimes three or four, service areas for each of the city departments (such as Police, Education, Health, Hospitals, Welfare). None of these coincides with each other or with the Community Planning District (see Figure 1). It is assumed that some of these departments will gradually reorganize and redistrict their service areas to coincide with the Community Planning Districts. At the present time, the latter are used as the basis of capital budgeting for the entire city.

The various districts produce a cobwebbing effect on the map. The number of different ways of carving up the city administratively makes it hard, not only to collect comparative data, but also to plan and implement programs. Moreover, the complex districting has profound effects upon the community's ability to organize and mobilize itself; the effects are equally far-reaching upon the frustrated and bewildered citizen. Frequently, the citizen's inability to take action on his own behalf is quietly dismissed as apathy or anomie; while in actual fact, the jurisdictional and administrative barriers to action are of a magnitude to daunt even the sophisticated professional. This fact has been established time and again by health, community action, and other programs that have provided advocacy help to their clients (7).

Sub-Areas in East Harlem

A survey (8) made by local organizations with professional assistance prior to the development of the OEO program suggested ten sub-communities or sub-areas in East Harlem. They are (see Figure 2):

1. The East Harlem Triangle
2. Mount Morris
3. Triboro
4. El Barrio
5. Aguilar
6. Jefferson
7. Hell Gate
8. Carver and East

9. Lexington
10. Metro North

There may be some question now as to how viable these are as sub-communities, but their names are generally known and accepted in East Harlem. Each of the areas has its own distinct qualities, physical features, and population characteristics, some of which are undergoing change.

According to the 1960 census, and some limited updating estimates made since then, the white population is concentrated mainly in the southern portion of East Harlem, in Carver and East, Lexington, and Metro North. There is another pocket of white (Italian) residents in the Triboro area. The Puerto Rican population predominates in the central portion of East Harlem, in Aguilar, El Barrio, Hell Gate, Metro North, Jefferson, and part of the Triangle. The Black population is concentrated in the northwest portion of East Harlem, in

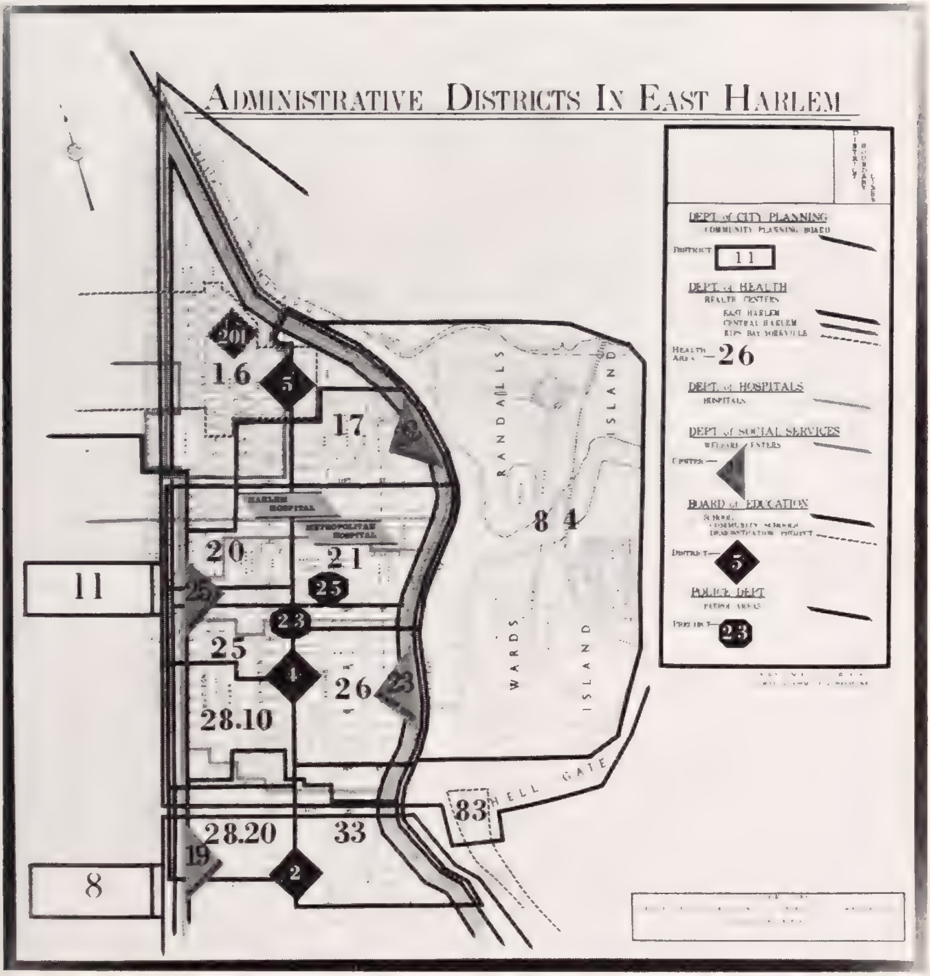
ADMINISTRATIVE DISTRICTS IN EAST HARLEM
DISTRICT BOUNDARY LINES
DEPT of CITY PLANNING
COMMUNITY PLANNING BOARD
DISTRICT 11
DEPT of HEALTH
HEALTH CENTERS
EAST HARLEM
CENTRAL HARLEM
KIPS BAY YORKVILLE
HEALTH AREA 26
DEPT of HOSPITALS
HOSPITALS
DEPT of SOCIAL SERVICES
WELFARE CENTERS
CENTER
BOARD of EDUCATION
SCHOOL
COMMUNITY SCHOOLS
DEMONSTRATION PROJECT
DISTRICT 5
POLICE DEPT
PATROL AREAS
PRECINCT 23
201
16
5
17
HARLEM HOSPITAL
METROPOLITAN HOSPITAL
20
21
25
23
11
25
4
26
28.10
23
RANDALLS ISLAND
WARDS ISLAND
84
HELL GATE
83
28.20
33
19
2
8

FIG. 1. Administrative Districts in East Harlem.

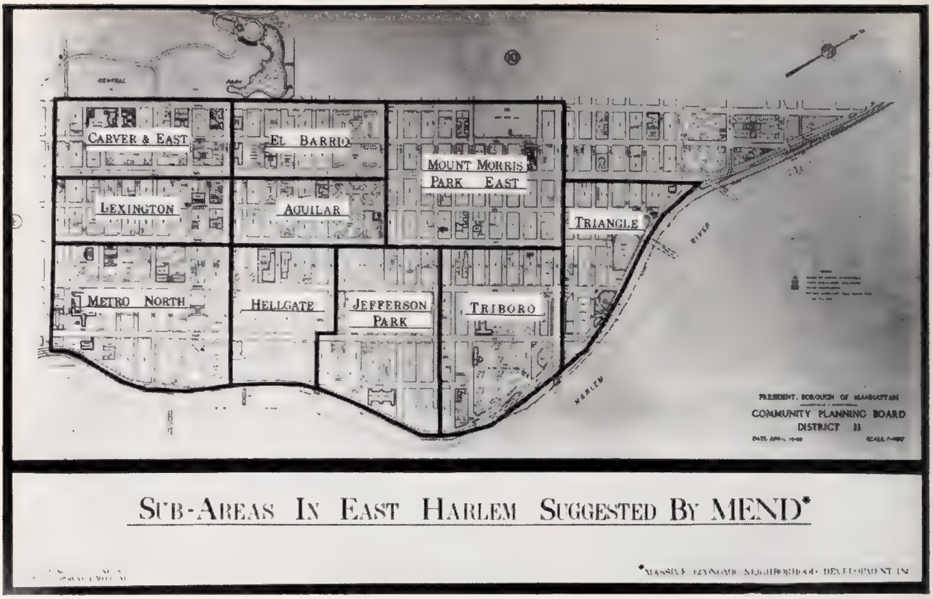
CENTRAL
CARVER & EAST
EL BARRIO
MOUNT MORRIS PARK EAST
LEXINGTON
AGUILAR
TRIANGLE
METRO NORTH
HELLGATE
JEFFERSON PARK
TRIBORO
HARLEM
RIVER
PRESIDENT, BOROUGH OF MANHATTAN
COMMUNITY PLANNING BOARD
DISTRICT 11
SUB-AREAS IN EAST HARLEM SUGGESTED BY MEND*
*MASSIVE ECONOMIC NEIGHBORHOOD DEVELOPMENT INC

FIG. 2. Sub-Areas in East Harlem Suggested by MEND (Massive Economic Neighborhood Development).

the western part of the Triangle, and Mount Morris. There is some evidence which suggests a movement of Blacks from Central Harlem into the central part of East Harlem.

As to population density, the least dense areas in East Harlem are portions of the Triangle and Triboro; the most densely populated sections are the southern part of the Triangle and Jefferson.

Indices of income reveal that a decade ago, the central section of East Harlem was the most economically deprived sector. This area, from Fifth Avenue east to the River and from about East 112th Street south to East 99th Street, covers parts of El Barrio, Aguilar, Hell Gate and Metro North. It had the highest incidence of welfare families, the lowest median income, the lowest mean school years completed, the highest rate of unemployment, and the highest rate of substandard housing (**9**).

Land Use

East Harlem is a predominantly residential community with areas of concentrated commercial and industrial activity and some areas of mixed use. The strongest commercial areas are located on 125th Street, in Franklin Plaza at Third Avenue and East 106th Street, and the Park Avenue Market-116th Street area. The market is located beneath the Penn Central Railroad tracks from 110th to 116th Street. The north-south avenues, particularly Third Avenue, contain shops and offices which are mainly ground-floor establishments.

The east-west streets have scattered commercial frontages. These are mainly candy stores, small grocery stores, delicatessens, and "bodegas." A good many of them are vacant, which is characteristic of East Harlem and in contrast to Central Harlem (10). In addition to their more customary use as storefront churches, many of these stores are being converted for use by a variety of agencies and organizations. There are few vacant parcels of significant size in the area; however, there are a number of small, scattered vacant lots throughout the community.

The East River Urban Renewal program will transform the area between East 107th Street and East 111th Street from industrial to residential use. The industrial uses fronting the East River have no relation to the river.

Recreation

The lack of recreational space, and the under-utilization of Central Park, have already been noted. The 20-acre Mount Morris Park is undergoing renovation. Jefferson Park with 14 acres is the only outdoor recreation center which includes a public swimming pool and a playing field. Athletic space for teenagers is a notable deficiency of the area. Space along the river in the East Harlem Triangle has potential for this type of recreational development, but it is not centrally located.

The stadium at Randall's Island, with access via the Triboro Bridge, is used for athletics, staged pageants, and similar activities. Ward's Island is accessible by a foot bridge at East 105th Street, and is used by the people of that neighborhood as a pleasant park and picnic area. Local residents have worked with the Department of Parks in the recreational planning for Ward's Island. Both islands will continue to be developed for regional recreation and institutional purposes. If they are to reach their full potential, increased land fill and improved access will be needed.

Transportation

East Harlem is easily accessible by all means of public and private transportation, being served directly by bus, subway, and commuter rail lines. The Triboro, Willis Avenue, and Third Avenue Bridges, the Harlem River Drive, and the Franklin D. Roosevelt Drive provide automobile access to and from all parts of the metropolitan area. The intersection of East 125th Street and Lexington Avenue is both an express subway stop and bus transfer point; the Penn Central station is one block west.

Rapid vehicular access is found on First, Second, and Third Avenues. The north-south avenues are served by four bus lines, and there is crosstown bus service at 96th, 110th, 116th, and 125th Streets. There is also a shuttle service from Fifth Avenue to the East River which was obtained through local community effort when Franklin Plaza was completed. Nevertheless, for some of the area residents, crosstown movement is difficult. Many find it more convenient to use bus and subway along the major north-south arteries to obtain medical care and other services south of East 96th Street.

Housing

The concentration of 13 public housing projects dominates the housing picture in East Harlem when compared to other areas of the city. These projects occupy some 67 of 248 city blocks, or almost one-third of the entire area. With 20 additional blocks assigned for Neighborhood Conservation and 43 blocks for Area Services, some 52 per cent of the entire area is being conserved, protected or developed under public auspices. Of the remainder of the housing stock, 65 percent are Old and New Law tenements and nearly half of these are either deteriorated or dilapidated.

Public housing projects provide almost 17,000 dwelling units housing about 50,000 persons or almost one-third of East Harlem's population. In 1968, approximately 52 percent of these units were occupied by Blacks, 47 percent by Puerto Ricans, and one percent by whites. These public housing developments are supplemented by 1,635 dwelling units in the Franklin Plaza cooperative, 1,232 units in the Riverton houses, and 624 in the Riverhead cooperative.

Education

There are 28 public schools in East Harlem: two are high schools (Benjamin Franklin and Manhattan Vocational); five are junior high schools; one is an intermediate school; and twenty-two are elementary schools. There are, in addition, eleven parochial schools, the largest of which are St. Francis de Sales and St. Cecilia's.

The construction of about 14 new public schools in less than ten years has not only improved the physical school plant, but has reduced overcrowding in East Harlem, particularly in the elementary schools. This adequacy of the educational physical plant is the result of the prolonged efforts by local leadership which competed successfully against other areas in the city for scant resources.

Religion

In East Harlem there are 135 places of worship: nine Catholic churches, 121 Protestant churches, two Orthodox churches, and three Jewish synagogues. The two largest groups in the area are Baptists and Pentecostals. Today, East Harlem closely resembles the city so far as the proportion of Catholics is concerned, with almost 50 percent; it has 35 percent Protestants, compared with the city's 27 percent, with the Jewish group a good deal smaller than the city average (11).

When the Irish and Italians came to New York they, like other Catholic immigrant groups, soon brought their own priests with them or sent for some from their country of origin. Thus, national Catholic churches tended to grow up wherever there was an ethnically homogeneous group large enough to support them.

The Puerto Ricans migrating to New York City in the thirties and forties, however, did not bring priests with them. La Milagrosa in East Harlem was the Spanish-language church of the Archdiocese; but the priests were of Spanish rather than Puerto Rican origin, and the parishioners came mainly from a higher socioeconomic class than the Puerto Rican immigrants. The latter did not feel particularly at home in this setting and so they started to attend the local Pentocostal churches and to form new ones of their own (12).

Some Puerto Ricans later joined other Protestant denominations, while others returned to established Catholic churches. St. Cecilia's has the largest number of Puerto Rican parishioners in East Harlem; but Puerto Ricans also attend Our Lady of Mount Carmel in the northern part of the area—a church attended by the Italian community—and St. Francis de Sales in the south, which also serves a number of Irish parishioners.

In 1949, The Union Theological Seminary established the East Harlem Protestant Parish. A number of small churches, some of them storefront, were set up with different denominational support. This constituted an attempt by the Protestant ministries to make their witness more relevant to life in the urban community. The Parish addressed itself to the problems of poor housing, narcotics, unemployment, and education.

Political and Social Factors

East Harlem is generally perceived nowadays as a Puerto Rican or predominantly Puerto Rican district. Nevertheless, the influence of the Italians outweighs their dwindling numbers and persists with remarkable tenacity. It is particularly apparent in the businesses and political activities of community life. Italians own many of East Harlem's most viable business concerns including liquor stores, bars, and other establishments—even when these are located in sections in which few, if any, Italians still reside. These businesses, unlike others in East Harlem, are rarely used as "hangouts" by antisocial teenage groups; nor were they so used by the gangs in the fifties.

Politically, East Harlem is a heavily democratic area. Its ties to Tammany Hall in the past are well known. Although the people of East Harlem did not, like those in middle-class Yorkville, become active participants in the Reform Movement, the latter has had profound implications for East Harlem politics. The Reform influence has broken the back of the old political structure in New York City and has thereby created a political vacuum. It is obvious that East Harlem has reached a turning point in its political life.

In 1960, Manhattan had five Congressmen, but after the 1960 census one of the congressional seats was lost, which meant that East and Central Harlem had only one man to represent them—Adam Clayton Powell. Although the Puerto Ricans and Negroes number one half of the population of Manhattan, they hold only one of the four seats in Congress. Gerrymandering of the political districts has indeed deprived the East Harlem community of its full complement of local councilmanic, state legislative, and congressional representation (13).

Like some other urban low-income communities, East Harlem has always been a center of illegal activities which become the interstitial tissue of the community's life. From without as well as from within the community, it is recognized that it is predominantly poor people who play the numbers, and most of them play because they are desperate for money and feel this is one of the few possibilities open to them (14).

Often, programs planned to improve local conditions are stopped in their tracks when they run into this factor. Lack of cooperation on the part of tenants or local residents is often viewed by the outsider as apathy; but it may well be due to a reluctance to have official inspections made in apartments where illegal activity is conducted. Indiscriminant picture-taking is never welcomed, is often misinterpreted, and sometimes brings serious unanticipated consequences to the photographer. The law of silence, or "omerta," affects the community's attitude to, and relationship with, the police. For this law is translated into the old American virtue of "minding one's own business": no one has seen the crime committed in one's presence, and cooperation with the police makes one a marked man. This attitude is reflected in the remark of a woman in her sixties who was a numbers runner. When asked by the writer what she would do if caught, she replied "I'd say to the judge, 'Judge, you'd take a 6 to 1 chance yourself.' "

Narcotics, policy, gambling, and other illegal activities still flourish openly. More recently, there seems to be a resurgence in the number of candy stores, pizzerias, delicatessens, restaurants and other small shops that have opened and which apparently operate as "fronts." East Harlem has been the base for one of the Cosa Nostra's most powerful "families."

Nevertheless, it is widely recognized that the East Harlem community has many strengths. Public officials deal with its leaders with care and respect. Local leaders have obtained city- and nation-wide recognition. The activities of its residents and the programs which have been generated locally have appeared not only in the local press but in such diverse publications as the *New York Magazine* (15), *Time Magazine* (16), *The Saturday Review* (17), *The New York Times Magazine* (18), a Polish and Russian edition of *America, U.S. Information Agency* (19), the *Johns Hopkins Journal* (20), and the *New York State Psychologist* (21). *Traveller's Times Posters* have distributed car and bus card posters of a local hotdog vendor, who is active in remedial education, throughout the major cities of the United States. East Harlem has been the locale of a number of movies: *The Lost Weekend, The Window,* and, more recently, *Up the Down Staircase* and *Popi.* In real life, the young boys in this latter film are in the Day Care program, and the mother of one is a local PTA president. The older boy has just returned from Australia where a second film was made.

The Future

The late thirties and early forties marked the period of East Harlem's greatest physical deterioration. Since that time, the housing stock has gradually improved. Although the bulk of the replacement has been public housing, our review has shown that there has been increasing interest and activity both in rehabilitation and construction on the part of local groups. These efforts, both public and private, have been strengthened and supported by new governmental tools and aids found in the successive Housing Acts and administered by the Department of Housing and Urban Development (HUD).

The Model Cities Program, now in its second year, is a new effort at comprehensive planning to restore and revitalize large sections of urban blight and deterioration. The administrative, technical, and operational problems of such large scale programs means a gradual and often slow change with many unanticipated delays. It will, therefore, be some time before we can evaluate their impact.

Since East Harlem reached "the bottom" physically in the thirties and early forties, the general feeling has been that the community is "on its way up," or, at least that it will not become worse. An encouraging sign has been the ability of the leadership to work together effectively on housing and school problems. At this point in time, it is too early to know how the competition for "poverty" funds, the conflict and polarization of the Black and Puerto Rican groups, or the movement toward community control will affect life in East Harlem in the near future.

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Reflections on Latent Viruses—A New Definition of an Infectious Agent

SHALOM Z. HIRSCHMAN, M.D.

Introduction

During the past few years there has been much interest in latent viruses with resultant exciting discoveries. The data derived from these studies have broad biological implications which suggest a new definition of an infectious agent. In this communication, two classes of latent viruses will be considered, the RNA-containing tumor viruses and the "slow growing" viruses. Indeed as the bits of information as to the nature of the RNA-containing sarcoma and leukemia viruses accumulated they seemed to challenge accepted mechanisms of replication of the RNA-core viruses. Recent biochemical studies on the replication of the nucleic acid of these viruses have substantiated their uniqueness and uncovered new modes of nucleic acid synthesis. Once the mechanism of replication of the RNA-containing tumor viruses is solved, much insight into the mechanism of carcinogenesis and infection in general will be gained.

It is necessary to define the type of virus latency which will be discussed in this paper. There are two broad types of viral latency. In a review of latent virus infections in primate tissues Hsiung (1) implied that, based on reconstruction experiments, the latent infections in these tissues were due to quantities of virus initially too small to detect until the virus was allowed to replicate to assayable levels. This is not the type of viral latency considered in this paper. The viral latency with which we will be concerned implies the presence of virus in a potential but nondetectable and nonreplicating form transmitted from generation to generation of host cell.

Latency of Murine Leukemia Viruses

Aaronson, Hartley, and Todaro (2) noted that BALB/c mouse embryo cells maintained in tissue culture on a schedule of rapid transfer at high cell density developed tumorigenic lines that lost contact inhibition of cell division. After several months in culture some of these lines released a murine leukemia virus like that found spontaneously in adult BALB/c mice (3). Aaronson et al (2) argued that based on reconstruction experiments these observations pointed to the presence of a latent leukemia virus in BALB/c cells. These authors claimed that their reconstruction experiments indicated that the murine leukemia virus was latent because the information necessary to make the virus was repressed and not because the amount of virus initially present was too little to detect. Based on this type of experiment, Huebner and Todaro (4) developed the hypothesis of the "oncogene", i.e. tumor virus genes, behave more like cellular

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From the Division of Infectious Diseases, Department of Medicine, Mount Sinai School of Medicine of The City University of New York, N.Y. 10029.

Abbreviations: RNA = Ribonucleic acid; DNA = Deoxyribonucleic acid.

genes than like infectious viruses. Consequently horizontal transmission as a natural mode of infection would be less important than the natural occurrence of cancer. The hypothesis implies that the occurrence of most cancer is a natural biological event determined by spontaneous and/or induced derepression of a specific viral "oncogene(s)."

The observation of the latency of the murine leukemia viruses is certainly not new. As early as 1951 Gross (5) suggested that the murine leukemogenic agent is transmitted vertically from one generation to another as in chicken lymphomatosis. Later he presented evidence which indicated that normal healthy mice of the low leukemic C3H Bittner line may carry the leukemogenic agent in a masked and usually nonpathogenic state (6). When triggered by ionizing radiation this agent became pathogenic and caused leukemia. Lieberman and Kaplan (7) demonstrated a similar phenomenon in C57BL mice. The leukemogenic factor, which was latent in the untreated mice, was activated by ionizing radiation and, in some respects, was considered to resemble the bacteriophage of lysogenic bacteria.

Latency of Murine Sarcoma Viruses

The Moloney sarcoma virus (MSV[M]) may exist in a silent, nondetectable state in mouse embryo cell (MEF) cultures (8). Mouse embryo cells infected with a defective MSV(M) isolate diluted beyond the focus-producing endpoint showed no focus formation at eight days of incubation. However, further passage of these cells split into daughter plates yielded MSV(M) foci after six days of further incubation (8). Reconstruction experiments indicated that MSV(M) focus formation should have been detected in the infected parent cells.

The reversion of MSV(M) to a nondetectable state may also be induced in infected cultures through the use of cytosine arabinoside, a potent inhibitor of DNA synthesis (8). When secondary MEF cells were infected with MSV(M) and fed with medium containing cytosine arabinoside for 16 hours, at which time the medium containing the inhibitor was removed and the infected cells were fed with fresh medium containing deoxycytidine, no virus was detected during the first 48 hours of incubation. However, 1.7×10^3 Focus Forming Units (FFU) per ml of virus were detected by 7 days of incubation. Reconstruction experiments with nontreated cultures yielding similar quantities of MSV(M) indicated that virus should easily have been detected at 48 hours (8). Thus under conditions inimical to viral growth MSV(M) may exist in a nondetectable or latent form and this latent state may be produced under proper conditions in the laboratory.

Mechanisms of Replications that May Account for the Latency of the Murine Leukemia and Sarcoma Viruses

Before considering mechanisms of replication that may account for the latency of MLV and MSV(M) some of the curious biochemical properties of these viruses must be appreciated. Unlike other RNA-containing viruses (9) the murine and avian sarcoma and leukosis viruses require DNA synthesis for replication and transformation (8, 10–12). Temin (13) had speculated that a DNA template is used for the replication of these viruses and that a DNA provirus existed. Indeed, it had been shown that the Moloney murine leukemia and sarcoma viruses stimulated DNA synthesis in mouse cells in tissue culture (14). When the viral growth curve of MSV(M) was determined in conjunction with the effect on DNA synthesis, the stimulation of DNA synthesis was found to occur during the logarithmic stage of viral growth (14). It is not yet known whether the DNA synthesized was viral-specific or cellular DNA.

At this point it was difficult to envisage how the type of viral latency proposed by Aaronson et al (2) for the murine leukemia viruses could arise. If whole or partial virus particles were present in the cells in a noninfectious and nonreplicating form, then repeated cell passage should, if anything, successively have diluted out the virus particles. Similar arguments hold for nonreplicating pieces of DNA and RNA. Although Biswal and Benyesh-Melnick (15) discovered minus RNA strands in the nuclei of the 78A1 rat embryo cell line transformed by the Murine sarcoma-leukemia virus complex (MSV-MLV) it was difficult to envisage how the RNA of the latent virus could replicate synchronously or asynchronously with the host cell. Certainly a lysogenic RNA-containing bacteriophage had not yet been found in nature (16). In contrast to other RNA-containing viruses the minus RNA strands of MSV-MLV were found in the nucleus and not in the cytoplasm (15). Biswal and Benyesh-Melnick (15) suggested that a DNA intermediate was not required for the replication of MSV-MLV, as postulated by Temin (13) for Rous sarcoma virus, but that cellular gene function was necessary for viral replication. Yet these authors could not account for the latency of these viruses.

It was obvious that if, indeed, the RNA-containing tumor viruses were replicated from a DNA template then this DNA, in the latent state, might replicate synchronously or asynchronously with the cell analogously to a bacterial episome (16, 17). Viral DNA might even integrate with the host cell DNA as in bacterial lysogeny (16). However, such a mechanism would have violated the then accepted direction of nucleic acid synthesis, that is, DNA synthesizes RNA which then codes for the synthesis of protein. Even if one postulated that the viral RNA of the tumor viruses coded for enzymes which synthesized the viral DNA, one still had to account for the origins of the template from which the viral RNA was synthesized.

Here the problem stood until the exciting discovery of Temin and Mizutani (18) and Baltimore (19) that the RNA-containing tumor viruses did contain activity indicating the presence of a RNA-dependent DNA polymerase. These discoveries shook the world of molecular biology. Now it was apparent that the synthesis of nucleic acid was symmetrical, that is, DNA and RNA could code for each other. The biological implications of this discovery are immense. Certainly the symmetrical synthesis of nucleic acid would afford cells with very fine tune controls of gene expression. As of this writing the following enzymatic activities have been found in RNA-containing tumor viruses: 1) The above mentioned RNA-dependent DNA polymerase; 2) A DNA-dependent DNA polymerase (20, 21); and 3) An endonuclease which splits DNA into smaller chains (21). Mizutani, Boettiger, and Temin (21) also hypothesized that a ligase must be present in the RNA-containing tumor viruses which ties together the small chains of DNA which seem to be synthesized by the RNA-dependent DNA polymerase into a long molecule.

It is thus apparent that the RNA-containing tumor viruses are indeed synthesized from a DNA template or provirus as originally postulated by Temin (13). Since RNA-containing tumor viruses have been isolated from many mammalian species and the RNA-dependent DNA polymerase activity has been found in all RNA-containing tumor viruses examined an exciting new area presents itself for an attack on the problem of a cure for cancer. If the enzymes discovered in the RNA-containing tumor viruses are unique to these viruses then the possibility exists that these enzymes may be preferentially inhibited when the virus infects host cells. Of course, workers in the field are now busily seeking evidence of this enzyme activity in human tumor cells (22). These studies may shed light on the cause of leukemia and other cancers in humans.

What Kind of Infection is Cancer?

The exciting data discussed in the previous paragraphs were gathered in vitro, this is, with isolated and purified virus in the test tube. Nothing is known about the functions of these enzymes in vivo, that is, in infection of cells and the resultant causation of tumors.

We can now speculate on how a tumor virus might replicate once it has entered a susceptible host cell. In the simplest model the virus, once in the cell, would be uncoated, and in the nucleus of the host cell the viral RNA would replicate DNA via the RNA-dependent DNA polymerase. Then more DNA would be replicated via the DNA-dependent DNA polymerase and the DNA would then code again for viral RNA either via a hitherto undiscovered viral DNA-dependent RNA polymerase or the DNA might use the cellular DNA-dependent RNA polymerase which is present in the nucleus. The host cell would either be killed by the virus or would be transformed into a tumor cell in which the virus would continue to replicate, although the tumor cells continued to divide. Of course, virus would be transferred to the daughter cells of this division. In some cells the DNA synthesized from the viral RNA would integrate into the host cell chromosome and replicate with the host cell genome. The cell could thus be stably transformed into a tumor cell as occurs with the DNA tumor viruses (23); or the DNA, though integrated with the host cell chromosome, may be repressed through such integration and may not be expressed. In this state the RNA tumor virus would now be latent in the host cell. Suitable stimuli such as X-irradiation or rapid transfer in tissue culture would then serve to induce the latent DNA to an active state. Among the many questions to be answered as to the replication of these viruses are a) Does the viral DNA always integrate into the host genome during the replication cycle or can the viral DNA replicate as a separate entity?; b) Does the viral DNA code for viral RNA through a virus specific DNA-dependent RNA polymerase or does it use the RNA polymerase of the host cell?; c) What determines the induction of the latent state? It would seem that tumor viruses normally enter a latent state on infection of susceptible host cells because cancer is not easily spread horizontally. The work of Aaronson et al (2) indicates that all cells are potential producers of tumor viruses and that the genes which code for the RNA of tumor viruses are widely prevalent amongst mammalian species so that integration of viral DNA into host cell genome is a stable event; d) Why does the tumor virus need a DNA-dependent DNA polymerase? Would it not be sufficient for the viral RNA to code for DNA which then would code for the RNA? Perhaps the viral RNA is so unstable that the DNA-dependent DNA polymerase is needed to amplify the synthesis of virus; e) A more fundamental question is why does this RNA virus take a circuitous route for its replication unlike the other RNA viruses? Is it again because the RNA of the viruses is so unstable that a more stable intermediary is needed?; f) How does the virus transform a cell into a tumor cell?; g) Does oncogenic transformation necessitate integration of some part of the viral genome into the host cell genome?

It is interesting to reflect on the possible origins of mammalian cancer genes. Much of the DNA of mammalian cells is inactive or "switched off" (24). These inactive genes are present in the dense chromatin of the nucleus (24). It has been suggested that proteins such as the histones which are found in conjunction with nucleic acid in the cell nucleus are combined with the DNA to keep it inactive (25, 26). Perhaps this inactive DNA contains some deleterious genes. Amongst these genes could be those that code for the RNA-containing tumor viruses. Under suitable conditions these tumor virus genes could be activated as discussed above. Thus cancer would be an endogenous rather than an exogenous infection. Indeed, when the virus infects the susceptible cell the DNA which is synthesized from the viral RNA might activate or derepress the tumor gene which is present in the cell by combining with the repressor proteins. Thus the virus could be self-inducing. Once derepressed the tumor gene could be expressed as transformation of the host cell to a tumor cell. Only one virion per cell would be necessary for the derepression of the tumor gene and one could then envisage a model in which a productive replication of virus would occur only when the DNA of the tumor gene is ejected from its integrated state in the host chromosome. This would account for the difficulty in detecting tumor viruses in the cancers of most mammalian species. Furthermore, the activation of a normally inactive part of the cell genome may give rise to a general interference with the normal control mechanisms of cell division (14).

The proposed models of the replication of the tumor viruses would account for: a) DNA dependence of RNA-containing tumor virus replication; b) the stimulation of DNA synthesis by these viruses; c) the presence of minus RNA strands in the cell nucleus; d) the spontaneous appearance of leukemia virus in adult mice; and e) the induction of leukemia viruses by X-irradiation.

The nonproducer (NP) state described for rat cells infected with the Murine sarcoma virus (27) may be a part of the spectrum of the latency of these viruses. A similar mechanism would account for the nonproducer cell infected with the Rous sarcoma virus (28). The NP cell may show some active virus (29) or contain internal virus antigen (28). This antigen was not demonstrable in the initial mouse embryo cultures of Aaronson et al (2) but was detected after MLV production began. Thus in the nonproducer cell the virus would be present in a partially repressed state, that is, the viral DNA would be able to code for the internal virus antigen but would have difficulty in coding for the viral RNA.

Next, one can speculate on the origins of the RNA-containing tumor viruses. Are these viruses a result of the activation of a normally inactive part of the mammalian genome as discussed above, that is, a part of the mammalian genome which gradually through evolution became inactivated because its functions were no longer necessary or became too crude as the particular species evolved? The activation of this DNA could then be deleterious to the host cell. Alternatively the DNA which codes for the tumor virus could have arisen from a series of unfortunate mutations. As a third possibility, perhaps mammalian cells carry tumor virus genomes through infections of the cells with tumor viruses and the resultant integration of the DNA of the tumor virus into the host cell chromosome in a stable manner. In this sense the original infection would always be exogenous. If tumors are due to exogenous infections ways might be found to "cure" the host cells of this exogenous DNA as occurs in the curing of bacteriophage DNA that has been integrated into the bacterial host cell genome.

Other Latent Viruses—Slow Growing Viruses

Since we have now found viruses which intimately depend on the host cell nucleic acid for their replication one can conjecture that infecting agents need not contain nucleic acid at all. Such an agent would then replicate by inducing host cell DNA, perhaps that DNA which is normally inactive, to code for the further reproduction of the infecting particle.

An exciting recent development in microbiology has been the study of the "slow-growing viruses" causing disease of the central nervous system. Scrapie "virus" infection in sheep, goats, mice and hamsters is a slowly evolving and uniformly fatal degenerative disease of the central nervous system characterized by a long incubation period and a protracted afebrile clinical course (30). In sheep the disease has a strong genetic component (31). The Scrapie agent is exceedingly resistant to heat and will not pass through a 27 mμ cellulose nitrate membrane (31). Interferon is not produced by Scrapie infection of the central nervous system (32). The buoyant density of the Scrapie agent in cesium chloride is about 1.32, not dense enough for a naked nucleic acid and too dense to contain a lipid coat (31). Alper, Hage, and Clark (33) found that the Scrapie agent is not inactivated by exposure to high doses of ultraviolet light of wave lengths specifically absorbed by nucleic acids. These authors suggested that the agent may be able to increase in quantity without itself containing nucleic acid. Furthermore, the data obtained from electron irradiation yielded a target size of 7 mμ (molecular weight circa 1.5×10^5) for the Scrapie agent, which is too small for a nucleic acid code (33). Koprowski (34), in fact, partially lumped the murine leukemia viruses together with the Scapie agent and related viruses because of similar biological properties.

Perhaps another infectious agent which does not contain nucleic acid already has been discovered. The Australia antigen which is present in cases of hepatitis (35) has not been found to contain nucleic acid. Yet Blumberg et al (35) claim that the epidemiological evidence points to the Australia antigen as the infectious agent transmitting hepatitis. In keeping with our previous discussion it can be proposed that the protein of the Australia antigen can induce or activate nucleic acid of the host cell genome to produce finally the proteins of Australian antigen. In this sense the Australia antigen would be infectious. It is interesting that in some populations susceptibility to chronic infection with Australia antigen may be genetically determined (36). It has been shown (37) that proteins can act to unzipper DNA. Thus one can envisage the activation of an inactive DNA by a protein. A somewhat similar situation may exist among the phages of Bacillus subtilis. The defective phage PBSX of B. subtilis will package only host cell DNA (38). This phage fails to form plaques on any known host. What is of interest here is that the phage protein packet can evert a specific effect on host cell DNA. The effects on the host cell genome exerted by mammalian protein packet viruses may be more complex and may involve replication of the protein packet by a self inductive mechanism. However, purified Australia antigen has not as yet been shown to transmit hepatitis and future developments in this field will be of great interest.

Conclusion

The study of latent virus mammalian infection is presently one of the most exciting fields of biology. A common property of these viruses is that they seem to depend largely on the host cell genome for their replication. In the study of latent viruses one descends the ladder of parasitism past the virus which contains directly replicating nucleic acid to a more primitive infectious particle (Fig. 1). Infectious particles may be only "packets" of proteins which induce host cell nucleic acid to replicate these packets. In fact, the boundary between an infectious so-called "living agent" and a toxic biochemical agent is entered. The elucidation of the problems herein discussed remains a great challenge. All avenues of inquiry, even those seemingly unconventional, must be considered.

Summary

The RNA-containing tumor viruses can exist in a latent and nondetectable form is the host cell. Viral replication may be triggered by X-irradiation of the host animal or rapid passage of host cells in tissue culture. Although these are RNA-containing viruses they require DNA synthesis for replication. It has recently been shown that these viruses contain an RNA-dependent DNA polymerase. Various models for the replication of these viruses that also account for their latent state are discussed. The RNA-containing tumor viruses seem to

Multicellular parasites—e.g. Ascaris lumbricoides, Phycomycetes
↓
Unicellular Parasites
↓
- a. Protozoa e.g. Entamoeba histolytica (many organelles)
  ↓
- b. Actinomycetales
  ↓
- c. Bacteria
  ↓
- d. Rickettsiaceae
  ↓
- e. Chlamydiaceae
  ↓
- f. Viruses
  ↓
  - 1. DNA—core virus
    ↓
  - 2. RNA—core virus
    ↓
    - a. self-replicating template (direct) e.g. Vesicular Stomatitis Virus
      ?↓
    - b. self-inducing RNA-core virus (indirect) e.g. Murine leukemia virus
  ?↓
  - 3. Self inducing "virus" protein "packet" e.g. ? Australia antigen, Scrapie agent

FIG. 1. Parasitic ladder descending from multicellular parasites with cells well differentiated for different functions to a particle composed, perhaps, only of protein and containing no nucleic acid.

depend intimately on the host cell genome for their replication. It is hypothesized that perhaps a "virus" need not contain nucleic acid at all but may be a "packet" of proteins which can induce normally inactive host cell DNA to reproduce these proteins. This process is termed replication by "self-induction." The Scrapie agent which is one of the "slow growing viruses" and Australia antigen may represent such infectious protein "packets."

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Septicemia Caused by a Microorganism of the Genus Erwinia

DONNA MILDVAN, M.D., EDWARD BOTTONE, M.S., SHALOM Z. HIRSCHMAN, M.D., AND ALBERT CORNELL, M.D.

The motile gram negative rods which are members of the genus Erwinia have long been known as phytopathogens (1–3). In 1965 Muraschi et al (4) first reported the isolation of Erwinia strains from human sources, recovering the organisms from throat cultures of two children and one adolescent. The authors concluded that Erwinia strains are normally saprophytic in man, but under stressful host conditions they might play a role as opportunists. Von Graevenitz and Strouse (5) isolated Erwinia from five wound infections in mixed culture; however, they presented no proof of the pathogenic role of the Erwinia isolates in these wounds. In 1967 Slotnick and Tulman (6) first demonstrated the presence of Erwinia as an opportunist in human infection when they repeatedly isolated an Erwinia species from an infected area of skin over the medial malleolus of a fractured ankle. Recently an Erwinia species was isolated in pure culture from a brain abscess (7).

A patient from whom an Erwinia species was isolated from blood cultures and whose clinical course indicated the pathogenic role of this organism is the subject of the present report. Bacteriological characteristics of Erwinia and the conditions under which this plant pathogen may become a human pathogen are discussed.

Case Report

Patient S. P., a thirty-eight-year-old white woman who had previously been in good health, was admitted to The Mount Sinai Hospital on June 19, 1970 with a history of nausea, vomiting, and right upper quadrant abdominal pain unrelieved by analgesics. These symptoms had increased progressively in severity over the preceding three weeks. The patient did not have fever, chills, jaundice or melena. Two years previously the patient underwent an abdominal hysterectomy for uterine fibroids.

Physical examination on admission revealed moderate tenderness in the right hypochondrium. Laboratory studies, which included the hemogram, urinalysis, serum electrolytes, blood urea nitrogen (BUN), calcium, phosphorus, uric acid, lactic dehydrogenase, albumin, globulin, alkaline phosphatase, bilirubin, and fasting blood sugar were all normal. The erythrocyte sedimentation rate (ESR) was 41mm per hour (Westergren) and the serum glutamic oxaloacetic transaminase (SGOT) was 55 international units. An oral cholecystogram failed to visualize the gall bladder and an intravenous cholangiogram revealed a stone

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From the Division of Infectious Diseases, Department of Medicine, The Mount Sinai School of Medicine of The City University of New York and the Department of Microbiology of The Mount Sinai Hospital, New York, N. Y. 10029. This work was supported in part by a grant (T01 AI0041-01) from the U. S. Public Health Service.

obstructing the cystic duct. A cholecystectomy was performed on July 2, 1970 and the stone was removed from the cystic duct. The common bile duct appeared normal at operation and was not explored. The gall bladder appeared to be inflamed. On the first postoperative day, the patient's rectal temperature rose to 102°F and the white blood cell count was 15,900 per mm^3 with 87 percent polymorphonuclear cells. Although no source for the fever could be determined, therapy with cephalothin was initiated. Over the ensuing three days, the white blood cell count returned to normal but fever to 102°F persisted. On the evening of July 6, the patient's rectal temperature rose to 106° and she had shaking chills. Physical examination showed a normal blood pressure, a well healing surgical wound, and no abdominal tenderness. Urinalysis and chest roentgenogram were normal. Kanamycin therapy was begun because of the lack of response to cephalothin, and on this therapy the fever lysed within forty-eight hours with marked clinical improvement. The temperature chart is shown in Figure 1. Two separate sets of blood cultures drawn on July 6 both grew out an organism that was identified as a member of the genus Erwinia sensitive to kanamycin and resistant to cephalothin. Although the white blood cell counts did not exceed 10,000 per mm^3 during the septic episode, the differential counts showed more than 80% neutrophiles, including 11 to 26% band forms. A ten-day course of kanamycin therapy was completed and the patient made an uneventful recovery. Cultures of urine, stool, gall bladder, sputum, and the surgical wound were all negative.

Bacteriology

The organism recovered from the blood cultures was an actively motile gram negative rod with rounded ends, producing yellow pigmented colonies on sheep blood (5%), chocolate, mannite, and endo agars. The pigment was confined to

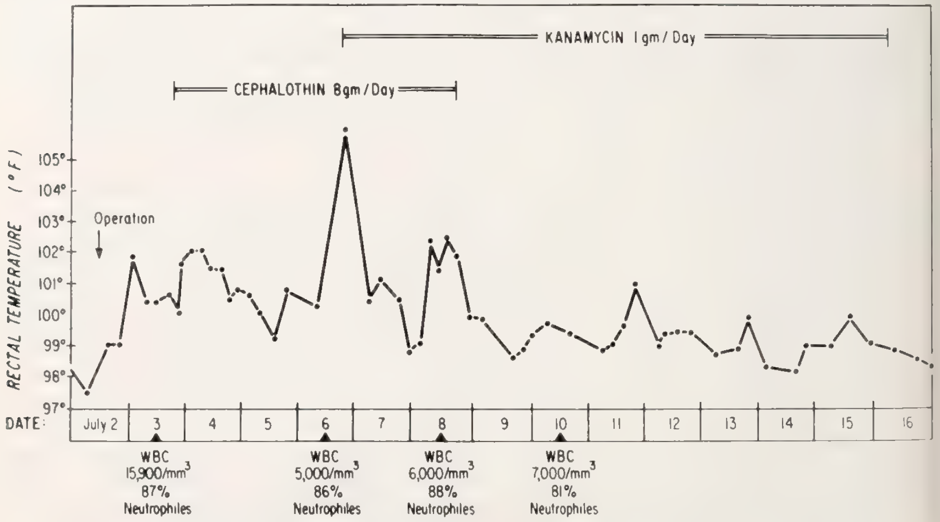

FIG. 1. Chart of patient's rectal temperatures showing dates of antibiotic therapy.

TABLE I

Characteristics of the Strain of Erwinia Isolated

Test	Result	Test	Result
Triple Sugar Iron Agar	acid/acid H_2S negative	Sorbitol	Negative
Citrate Utilization	Positive	Raffinose	Negative
Nitrate Reduction	Positive	Salicin	Positive
Urease Production	Negative	Inositol	Positive
Indole Production	Negative	Adonitol	Positive
Methyl Red Reaction	Negative	Malonate	Positive
Glucose	Positive	Lysine decarboxylase activity	Negative
Sucrose	Positive	Ornithine decarboxylase activity	Negative
Lactose	Negative	Arginine dihydrolase activity	Negative
Maltose	Positive	Symplasmata formation	Positive
Mannitol	Positive	Yellow pigmentation	Positive

the colony and did not diffuse into the surrounding medium. The pigmented colonies were highly mucoid, markedly adherent, and could be removed from the agar surface only with difficulty. The colonial morphology closely resembles that of Klebsiella.

The biochemical characteristics of the organism isolated are recorded in Table I. It fermented glucose, sucrose, maltose, and mannitol, producing acid but no gas; lactose fermentation was negative. Tests for decarboxylase, dihydrolase, extracellular deoxyribonuclease, urease, and cytochrome oxidase activity (Table I) were all negative.

Characteristic bacterial aggregates, "symplasmata," were observed by direct examination with phase microscopy of the condensation fluid of triple sugar iron (TSI) agar slants (Fig. 2).

Antibiotic susceptibility tests performed by a modified two-tube dilution method (8) showed the isolate to be sensitive to chloramphenicol, colistin, neomycin, polymyxin, streptomycin, and gentamicin, moderately resistant to tetracycline, and resistant to ampicillin and cephalothin. These data are listed in Table II and were similar to those previously reported (5–7).

Discussion

This case demonstrates that under certain conditions microorganisms of the genus Erwinia may cause severe infection in a previously helathy individual. It may be postulated that the patient had been harboring the organism as a saprophyte, and that the surgical manipulation may have resulted in blood stream dissemination of the organism. Alternately, the organism might have been introduced at the time of surgery. Several intriguing possibilities for the source of the Erwinia emerged from the patient's history since these organisms are primarily plant pathogens. On one occasion, and possibly on a second, prior

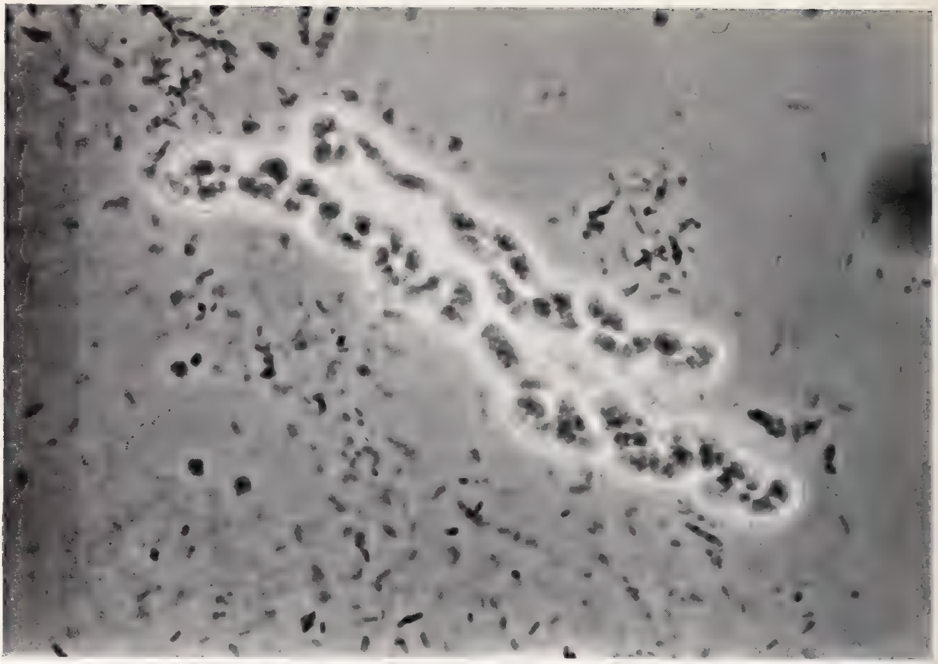

FIG. 2. Symplasmata, the characteristic bacterial aggregrates of Erwinia species observed by direct examination with phase contrast microscopy (original magnification × 400, × 9).

TABLE II

Antibiotic Susceptibility of the Erwinia Isolate Determined by the Two-Tube Dilution Method

Antibiotic	Concentrations Tested	Erwinia Isolate
	(mcg/ml)	
Ampicillin	5, 10	R
Cephalothin	7.5, 15	R
Chloramphenicol	7.5, 15	MR
Colistin	2, 5	S
Neomycin	10, 20	S
Polymyxin	2, 5	S
Tetracycline	2, 4	MR
Gentamicin	5, 10	S

S—Sensitive: Inhibition by the low and high antibiotic concentrations.
MR—Moderately resistant: Growth in the presence of the low concentration and inhibition by the high concentration.
R—Resistant: Growth in the presence of the low and high antibiotic concentrations.

to the patient's febrile illness, she pricked her finger on the thorn of a rose. In addition, the patient had worked in her garden prior to the onset of her illness but she denied exposure to noticeably diseased plants. After the isolation of the Erwinia was reported, the surgeon who performed the cholecystectomy recalled that he had tended his garden the day before the operation. The mere recovery of an organism from blood cultures does not establish its pathogenic role as recently pointed out by Gardner et al (9). However, the occurrence of very high fever with chills concomitant with the isolation of Erwinia from the blood cultures and the good response to therapy directed towards this organism lends support to its pathogenic role in our patient.

This is the first reported case of Erwinia septicemia. However, the taxonomic station of Erwinia species has been quite confused (2, 3, 10) and may have contributed, in the past, to their failure to be distinguished from the more commonly encountered Enterobacteriaciae, or to be designated as Erwinia isolates in the clinical laboratory. In some instances these organisms have been described under the name of Bacterium typhi flavum (11, 12). Indeed, as recently as 1968, Krishnan and Goldie (13) reported in an abstract the isolation of a yellow-pigmented bacillus from the blood of a 73-year-old man following gastric surgery and identified the organism as B. typhi flavum. Graham and Hodgkiss (14), comparing phytopathogenic Erwinia and chromogenic isolates from human sources, concluded on the basis of morphological, cultural and biochemical characteristics that B. typhi flavum should be classified as a member of the genus Erwinia.

It is probable that as an awareness of the morphologic and biochemical characteristics of Erwinia species becomes more widespread, recognition of their pathogenic role in human disease will increase and that these organisms will be added to the growing list of bacterial opportunists.

Summary

The first reported case of septicemia caused by a member of the genus Erwinia occurred in a 38-year-old woman following a cholecystectomy. The patient was treated with kanamycin and made an uneventful recovery. The morphologic and biochemical characteristics of this gram negative bacillary species are presented, and its role in human disease is discussed.

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The Diagnostic Microbiology of Lung Biopsy: Correlation with Viral Serology

SHALOM Z. HIRSCHMAN, M.D., BURT R. MEYERS, M.D., AND
STEPHEN J. MILLIAN, PH.D.

Lung biopsy, either open or needle biopsy, has been used for a long time as a method of diagnosing obscure diffuse pulmonary infiltrates (1, 2). Interest in the diagnostic value of these procedures recently has been heightened by the many reports of Pneumocystis carinii pneumonia complicating immunosuppressive, corticosteroid, and cytolytic drug therapy in such conditions as collagen diseases, organ transplantation, leukemias, lymphomas, and other solid tumors (3–6).

The reports on the diagnostic value of pulmonary biopsy procedures hitherto have focused on the pathological examination of the biopsied tissue. Little emphasis has been given to the diagnostic value of careful bacteriologic and virologic culture of the biopsied specimens. Furthermore, there have been almost no reports of extensive viral serologic studies in conjunction with the lung biopsies.

We recently have studied eleven patients who underwent open lung biopsy because of undiagnosed diffuse pulmonary infiltrates. From all these patients, pieces of tissue were carefully cultured for bacteria, fungi, and viruses. Five of the patients also had extensive virologic serological investigations at the time the biopsies were performed. The diagnostic results achieved in these patients are presented in detail.

Materials and Methods

Clinical Material

The eleven patients studied in this report were seen on the various wards of The Mount Sinai Hospital. Some of the pertinent clinical features of these patients are given in Table I. All had diffuse pulmonary infiltrates, most often as a complication of an underlying disease.

Lung Biopsy and Culture of Tissue Specimens

All the patients underwent an open lung biopsy during which four pieces of tissue were removed. One piece was used for pathologic examination including methenamine silver stains for Pneumocystis carinii, one for bacterial and fungal cultures, one for mycobacterial cultures, and one for viral cultures. Direct

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From the Division of Infectious Diseases, Department of Medicine, Mount Sinai School of Medicine of The City University of New York; and the Virus Diagnosis Service, Bureau of Laboratories, New York City Department of Health.

TABLE I

Clinical Features

Patient, Sex, Age	Underlying Disease	Salient Symptoms	Salient Signs	Drugs	WBC (and Differential)	Chest X-ray	Lung Pathology
B.R. M 8	Acute lymphatic leukemia	Fever—104°F dyspnea, cough	Tachypnea, no rales	Methotrexate Prednisone	9,000 (44 mature poly's 28 band forms 20 lymphocytes 2 monocytes 6 atypical lymph's)	Diffuse bilateral interstitial infiltrate	Interstitial pneumonitis, alveolitis, granulomata with multinucleated giant cells
J.P. F 10	Acute lymphatic leukemia	Fever 105°F, cough, diarrhea	No rales	Methotrexate 6-mercaptopurine	6200 (43 mature poly's 29 band forms 21 lymphocytes 6 monocytes)	Diffuse bilateral interstitial infiltrate	Interstitial pneumonitis, epithelial desquamation and proliferation, thickened alveolar septa
H.B. M 65	Chronic Lymphatic leukemia	Fever, dyspnea	Rales at lung bases	Leukeran® Prednisone	21,600 (10 mature poly's 8 bands 79 lymphocytes)	Diffuse bilateral interstitial infiltrate	Interstitial fibrosis, intra-alveolar fibrin and chronic inflammation
L.G. M 21	Hodgkin's Disease Stage IV	Severe dyspnea	No rales	Cytoxan® Prednisone	4,950 (95 mature poly's 41 lymphocytes 1 Eosinophile)	Patchy infiltrate left upper and lower lobes, and right lower lobe	Pneumocystis carinii pneumonia
N.J. M 49	Chronic lymphatic leukemia	Productive cough, weakness	Tubular breath sounds and rales at the left base	None	22,000 (52 mature poly's 7 band forms 30 lymphocytes 8 monocytes)	Bilateral lower lobe infiltrates	Leukemic infiltration of bronchial mucosa

M 42	ease Stage IVB		breath sounds right lung fields posteriorly, fine inspiratory and expiratory rales at bases	Vincristine Procarbazine BCNU	(62 mature poly's 24 band forms 13 lymphocytes 1 eosinophile)	infiltrate	Hodgkin's Disease
E.F. M 39	Chronic Myelogenous leukemia (blastic phase)	Spiking fever, tachypnea	No rales	Cytosine arabinoside Thioguanine	21,900 (8 mature poly's 21 band forms 38 blasts 43 lymphocytes)	Diffuse bilateral interstitial infiltrates	Interstitial pneumonitis, P. vivax in red blood cells
S.D. F 57	Not defined	Fever, swelling of left arm	Rales at left base	Keflin^{R} Streptomycin	17,2000 (87 mature poly's 11 band forms 2 lymphocytes)	Diffuse bilateral patchy infiltrates	Interstitial mixed infiltrates and fibrosis
C.K. F 49	Granulomatous hepatitis of unknown etiology	Fever, dry cough, dyspnea	Rales at right base	Prednisone Keflin^{R} Gentamicin	12,200 (45 mature poly's 10 band forms 35 lymphocytes 7 monocytes 2 eosinophiles 1 basophile)	Nodular infiltrates right upper and lower lobes	Abscesses due to Nocardia asteroides
M.W. F 63	Pulmonary adenocarcinoma, left upper lobe	Fever, dyspnea	Bibasilar soft rales	Cytoxan^{R}	11,000 (75 mature poly's 8 band forms 17 lymphocytes)	Segmental consolidation left upper lobe, diffuse interstitial infiltrate	Interstitial fibrosis, inflammation and epithelial proliferation
D.T. F 22	None	Fever, dyspnea	No rales	None	9,000 (60 mature poly's 9 band forms 26 lymphocytes 5 monocytes)	Diffuse granular infiltrate	Caseating granulomata with acid fast bacilli

smears were made from the piece of tissue taken for bacterial culture and stained with Giemsa, Gram, and Ziehl-Neelsen stains for microscopic examination. Pieces of tissue were cultured on blood agar, chocolate agar, Endo agar, liver-spleen agar, and in thioglycolate broth. The tissue specimen taken for mycobacterial culture was macerated and suspended in saline. Aliquots of the suspension were cultured on Lowenstein-Jensen and 7H10 solid media and in Dubos liquid medium. Virologic cultures were made by grinding a piece of lung with alumina in Hank's solution. After centrifugation, aliquots of the supernatant were inoculated into three tubes each of Rhesus monkey kidney, human embryo kidney, WI 38, and He La cell tube cultures. The cultures were carried for at least three weeks. After fifteen days a culture of the Rhesus monkey kidney cells was tested for hemadsorption with guinea pig red blood cells. Before being discarded all the cultures were tested for hemadsorption.

Serology

Paired sera were tested by conventional techniques in a microtiter system using commercial antigens. Titers are reported as reciprocals of the highest dilution which was positive. Serologic tests were performed for antibodies to Influenza A and B, adenovirus, respiratory syncytial virus, Psittacosis-Lymphogranuloma venereum, Herpes hominis, Cytomegalovirus, and Mycoplasma pneumoniae by complement fixation tests, and to Parainfluenza 1, 2, and 3 by hemagglutination inhibition tests.

Results

Bacteriology

In only three patients was a definite etiologic diagnosis of a treatable pulmonary infection made from material obtained at open lung biopsy (Table III). When an operation was performed on patient C.K., multiple abscesses, one of which was aspirated, yielding very thick, yellow pus were found. Both Gram and Ziehl-Neelsen stains of smears of this pus demonstrated an organism most compatible with Nocardia species. Culture of the pus yielded only Nocardia asteroides. Microscopic examination of a section of the biopsy specimen from patient D.T. showed granulomata with acid fast bacilli and P. carinii was seen in the specimen from patient L.G.

Virology

A virus was isolated from only one biopsy specimen. Patient M.W. had diffuse interstitial bilateral pulmonary infiltrates and Cytomegalovirus was cultured from the pulmonary biopsy specimen. However, intranuclear inclusions were not seen on pathological examination. Although no virus was cultured from the lung tissue obtained by biopsy from patient S.D., Herpes hominis virus was cultured from an autopsy specimen of lung obtained three weeks later.

Viral Serology

The results of viral serology tests are given in Table III. Four of five patients had elevated titers against Parainfluenza 3. One patient (M.W.) had elevated titers against both Parainfluenza 3 and Cytomegalovirus; and one patient (H.B.) had elevated Parainfluenza 3 titers, a sixteen-fold increase in titer against Herpes hominis and an elevated titer against Cytomegalovirus. Patient S.D. had a four-fold increase in titer against Mycoplasma pneumoniae.

Clinical-Pathologic Correlations

All the patients had fever and extensive pulmonary infiltrates at the time it was decided to perform an open lung biopsy in attempt to establish a diagnosis.

TABLE II

Diagnoses Established by Examination of Lung Biopsy Specimens

Patient	Diagnosis	Method of Diagnosis
L.G.	Pneumocystis carinii pneumonia	Pathologic examination
N.J.	Leukemic infiltration of bronchial mucosa	Pathologic examination
My.W.	Infiltration due to Hodgkin's Disease	Pathologic examination
E.F.	Plasmodium vivax malaria	Examination of stained slide of lung biopsy imprint
C.K.	Nocardia asteroides abscesses of lung	Culture of purulent material aspirated from lung abscess
M.W.	Cytomegalovirus pneumonitis (?Parainfluenza 3)	Culture of lung specimen, elevated titers (elevated titers)
D.T.	Miliary pulmonary tuberculosis	Pathologic examination, culture of lung specimen

TABLE III

*Viral Serology**

Patient	Date Serum Drawn	Titer
H.B.	7–8–69,	Parainfluenza 3–1:128; Herpes hominis–1:4; Cytomegalovirus 1:128
	7–17–69,	1:128; 1:8; 1:64
	8–1–69,	1:128; 1:64; 1:64
S.D.	8–15–69,	Mycoplasma pneumoniae–<1:4
	8–26–69,	1:32
J.P.	8–20–69,	Parainfluenza 3 – 1:64
	10–20–69,	– 1:64
B.R.	10–31–69,	Parainfluenza 3 – 1:128
M.W.	10–14–69,	Parainfluenza 3 – 1:128; Cytomegalovirus 1:128
	11–4–69,	1:128; 1:128
	11–26–69,	1:128; 1:128

* Only elevated titers are included in this table. All these patients had the complete serologic investigation.

Some of the clinical features of the patients at the time of open lung biopsy are given in Table I. Patients H.B., J.P., B.R., and M.W. had interstitial infiltrates, and microscopic examination of the lung sections showed interstitial mononuclear infiltrates and fibrosis consistent with a viral pneumonia. All these patients had elevated antibody titers to at least one virus known to be a pulmonary pathogen. Although patients H.B. and M.W. had elevated Cytomegalovirus complement fixation titers, intranuclear inclusions were not seen. Thus all four patients with presumed viral respiratory infections (Table III) had bilateral diffuse interstitial infiltration on chest roentgenogram and the microscopic pathology of the biopsy specimens was compatible with viral pneumonia. Since the patients had underlying diseases and were being treated with cytotoxic drugs, other clinical signs such as the white blood cell and differential counts and the erythrocyte sedimentation rate were not helpful in pointing to a diagnosis.

A biopsy had been performed on patient L.B. in 1968 for an obscure pulmonary infiltrate and Pneumocystis carinii was found. The patient was successfully treated with pentamidine isethionate. He was admitted one year later with fever and diffuse interstitial pulmonary infiltration. The lung biopsy showed interstitial fibrosis, and this time P. carinii was not seen. Patient C.K. had multiple nodular pulmonary infiltrates which developed while the patient was on steroid therapy. She raised no sputum and a biopsy was performed because of suspected fungal disease. The patient was placed on sulfisoxazole therapy for Nocardia asteroides but she died two months later with cerebral nocardiosis. Spiking fever and a diffuse pulmonary infiltrate developed in patient E.F. Giemsa stain of a smear of the pulmonary biopsy specimen showed P. vivax in the red blood cells. Microscopic section of the lung tissue showed interstitial pneumonitis. The fevers and the infiltrates remitted on chloroquine therapy. This is the first reported case of the diagnosis of malaria by lung biopsy! The patient had been in the Pacific theater during World War II but had not had malaria. It was assumed that he was infected with P. vivax via transfusion. Patient S.D. remained a diagnostic enigma even after a thorough autopsy and microscopic pathologic examination. This patient had been admitted to the hospital with a two-week history of erythema and swelling of the medial aspect of the left arm and the left axilla. She had spiking fevers and became dyspneic a week following admission. Chest roentgenogram showed diffuse interstitial infiltration. A diagnosis of her disease could not be established. Although she had an eight-fold rise in titer to Mycoplasma pneumoniae her clinical picture had not been previously associated with this organism. Herpes hominis was isolated from an autopsy specimen of her lung. However, this virus was not isolated from the lung biopsy specimen and she had not had elevated titers against H. hominis.

Lung biopsy afforded a diagnosis in seven of the eleven patients, in five through microscopic pathologic examination and, in two by culture of the lung specimens (Table II). In the patients with diffuse interstitial infiltration on chest roentgenogram, pathologic examination of the biopsy specimens was not diagnostic. However, the pathologic changes were compatible with viral infection. These patients had elevated viral serologic titers and Cytomegalovirus was isolated from one of the patients.

Discussion

Nine of the eleven patients in this report had an underlying neoplastic disease and therapy which increased their susceptibility to opportunistic pulmonary infections. There is no question that the prevalence of opportunistic pulmonary infections has been increasing (3). The number of fungus infections showed a fifteen-fold increase in the decade from 1950 to 1959 in two large hospitals in New York City devoted to patients who have malignant diseases (7). The importance of early lung biopsy for the diagnosis of obscure pulmonary infiltrates, especially pneumonia due to Pneumocystis carinii, in patients subject to opportunistic pulmonary infections recently has been emphasized by workers of the National Institutes of Health (4–6). Early diagnosis by lung biopsy increases the chance of successful therapy of opportunistic pulmonary infections (6).

Although the diagnostic value of bacteriologic and fungal culture of pulmonary biopsy specimens is evident in the literature, the diagnostic yield of viral cultures has not been given special attention (1, 2, 6). Furthermore viral serologic investigation has not been correlated with culture results and the pathology of the biopsied tissue. Four of our patients had nondiagnostic pathology and negative bacterial and fungal cultures. All had elevated serologic titers against a pulmonary viral pathogen, but a virus, the Cytomegalovirus, was cultured from only one of these patients. Four patients had elevated titers against Parainfluenza 3. The difficulty of culturing the respiratory viruses from patient material in conventional cell layers and the need for special culture techniques has recently been discussed (8). Although not diagnostic, the pathology in all five patients was consistent with a viral pneumonia. Perhaps the Parainfluenza 3 virus, like the Cytomegalovirus, is an important pulmonary opportunist in these types of patients. Interestingly, two patients had elevated titers against both Parainfluenza 3 and Cytomegaloviruses, and mixed pulmonary infection with both viruses may have been present. Although the four patients had elevated titers against Parainfluenza 3 or Cytomegalovirus, these titers were static. A four-fold or greater diagnostic rise or fall in titer was not demonstrated. However, the elevated antibody titers observed were consistent with recent infection.

It is not our purpose to discuss the relative merits of open versus needle biopsy of the lung. Open lung biopsy is the preferred procedure at The Mount Sinai Hospital because it allows direct examination of the lung for selecting the area of biopsy, yields more tissue for pathology and culture, and allows drainage of abscesses, if necessary. An abscess which yielded Nocardia asteroides was discovered at open lung biopsy in one of our patients. This patient had only a slight cough and did not produce sputum.

De Vita and his coworkers at the National Cancer Institute have reported a very high incidence of Pneumocystis carinii pneumonia in patients with underlying malignant diseases (4–6). In a recent review of their material, 44 percent of their patients had this infection (6). Only one of the eleven patients had evidence of P. carinii in this series of open lung biopsies. The explanation for the difference in prevalence of P. carinii in the two patient populations is not presently apparent.

Our experience indicates that the diagnostic yield of viral culture of lung biopsy specimens may be low. However, viral serology in patients with nondiagnostic pathology of the pulmonary biopsy tissue may be quite helpful in pointing to the etiology of an obscure pulmonary infiltrate. Although there is no specific curative therapy for most respiratory viruses there is much to be gained by establishing a viral etiology of an obscure pulmonary infiltrate. Such a diagnosis often spares the patient unnecessary and possibly dangerous antimicrobial therapy and may allay the fear a patient has of an undiagnosed disease.

Summary

Eleven patients had open lung biopsy for obscure pulmonary infiltrates complicating underlying diseases. Tissue specimens from each biopsy were cultured for bacteria, fungi, mycobacteria, and viruses. Five patients had extensive serologic testing for respiratory viruses and four of these patients had elevated titers against Parainfluenza 3. The diagnostic results achieved in these patients are presented and contrasted with previously reported patient series in whom lung biopsy was performed for the diagnosis of diffuse pulmonary infiltrates.

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Gas Chromatographic Determination of Urinary Testosterone and Epitestosterone Glucuronide

WALTER FUTTERWEIT, M.D., YOUNG ENG, M.D.,
AND SOLOMON I. GRIBOFF, M.D.

A method for the combined determination of urinary testosterone glucuronide has been described (1, 2). The purpose of this communication is to report a modification of this method to allow for separate identification and quantitation of these urinary metabolites.

The method has been modified in that the urinary extract is acetylated prior to gas chromatographic separation on an SE-30 glass column. Otherwise, the initial steps in extraction and preparation of the extract are unchanged. Briefly, C-1, 2-^{3}H-testosterone is added to a 100 ml aliquot of a 24-hour urine, which has been hydrolyzed with b-glucuronidase at pH 5. The urine is then extracted with ether, the phenolic fraction removed with 2N NaOH and a ketonic neutral extract prepared with Girard "T" reagent. The extract is chromatographed on a thin-layer plate employing benzene-ethyl acetate (3:2) as the solvent system. The zone corresponding to standard testosterone is eluted with acetone, and acetylated overnight with acetic anhydride and pyridine. The acetylated extract is spotted on a thin-layer plate employing a benzene-ethyl acetate (3:1) solvent system, and the zone corresponding to testosterone acetate is eluted with acetone. An aliquot of extract is counted in a Packard Tri-Carb liquid scintillation spectrophotometer employing a PPO-POPOP system.

The gas chromatographic system consisted of a Perkin-Elmer Model 881 dual column instrument with flame ionization detectors. The most suitable column for separation of epitestosterone and testosterone acetates was a 12-foot, 4 mm I.d. glass column packed with 2.8% SE-30 on Diatoport-S (mesh 80–100). The column was conditioned at 300°C for two hours without flow, and then at 255°C for 24 hours with nitrogen flow. Conditions for gas chromatography were as follows: column temperature, 250°C; detector block, 260°C; vaporizer temperature, 305°C.

Positive identification of testosterone and epitestosterone acetates was achieved employing infrared spectrophotometric studies* of the effluent collected from the peaks corresponding to the two acetates on the gas chromatographic column. The spectra obtained from the extracts of normal adult male urines corresponded to spectra of pure epitestosterone acetate and testosterone acetate.

Suitable aliquots of the extracts were injected into the gas chromatographic

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From the Division of Endocrinology of the Department of Medicine, Mount Sinai School of Medicine of The City University of New York, N. Y. 10029.

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TABLE I

Urinary Testosterone and Epitestosterone Glucuronide Excretion in 30 Normal Patients

Patient No.	Age	Sex	Testosterone (μg/24 hr.)	Epitestosterone (μg/24 hr)
1.	18	F	2	6
2.	21	F	2	9
3.	21	F	3	2
4.	25	F	2	2
5.	25	F	2	11
6.	29	F	2	5
7.	33	F	2	4
8.	37	F	2	2
9.	38	F	3	9
10.	41	F	4	4
11.	41	F	<2	5
12.	41	F	2	3
13.	45	F	5	4
14.	51	F	2	6
15.	57	F	<2	<2
16.	58	F	<2	5
				Av. T = 2.5 μg/24 (range-2–5 μg) Av. E = 5.0 μg/24 (range-2–11 μg)
1.	19	M	115	73
2.	22	M	98	71
3.	24	M	297	396
4.	30	M	119	111
5.	31	M	98	130
6.	35	M	50	107
7.	35	M	22	23
8.	41	M	83	73
9.	42	M	35	12
10.	43	M	18	15
11.	53	M	27	23
12.	56	M	29	25
13.	60	M	16	6
14.	77	M	17	19
				<45 years: Av. T = 94 μg/24 hrs. range: 18–297 μg/24 hrs Av. E = 101 μg/24 hrs. range: 12–396 μg/24 hrs. >45 years: Av. T = 22 μg/24 hrs. range: 16–29 μg/24 hrs. Av. E = 18 μg/24 hrs. range: 6–25 μg/24 hrs.

system by means of a Hamilton microsyringe following initial "saturation" of the column with 10 μg of testosterone and epitestosterone acetates. Peak responses in the extracts were quantitated from the resulting plot of peak height versus mass of standard testosterone and epitestosterone acetates, and correction for recovery of added ^{3}H-testosterone.

TABLE II

Urinary Testosterone and Epitestosterone Glucuronide Excretion in 27 Subjects with Various Endocrinopathies

Patient No.	Age	Sex	Diagnosis	Testosterone (μg/24 hr)	Epi-testosterone (μg/24 hr)
1.	17	M	Klinefelter's	17	3
2.	17	M	Klinefelter's	20	5
3.	17	M	Myotonic Dystrophy	58	19
4.	34	M	Myotonic Dystrophy	26	14
5.	35	M	Myotonic Dystrophy	34	13
6.	19	F	"Male Pattern" Alopecia	1	4
7.	22	F	"Male Pattern" Alopecia	2	9
8.	28	F	"Male Pattern" Alopecia	3	23
9.	30	F	"Male Pattern" Alopecia	15	14
10.	32	F	"Male Pattern" Alopecia	5	9
11.	17	F	Idiopathic Hirsutism	9	5
12.	18	F	Idiopathic Hirsutism	2	12
13.	19	F	Idiopathic Hirsutism	19	20
14.	19	F	Idiopathic Hirsutism	11	51
15.	20	F	Idiopathic Hirsutism	4	4
16.	22	F	Idiopathic Hirsutism	2	2
17.	23	F	Idiopathic Hirsutism	19	23
18.	25	F	Idiopathic Hirsutism	16	25
19.	27	F	Idiopathic Hirsutism	6	4
20.	30	F	Idiopathic Hirsutism	3	7
21.	31	F	Idiopathic Hirsutism	13	8
22.	37	F	Idiopathic Hirsutism	13	39
23.	44	F	Idiopathic Hirsutism	4	11
24.	45	F	Idiopathic Hirsutism	5	7
25.	21	F	Stein-Leventhal Syndrome	51	18
26.	21	F	Stein-Leventhal Syndrome	12	15
27.	23	F	Stein-Leventhal Syndrome	30	19

Urinary excretion of testosterone and epitestosterone glucuronide was measured in 30 normal subjects of various ages. The results are tabulated in Table I. Although testosterone glucuronide appears to be present in greater amounts than its epimer in normal adult males, epitestosterone is excreted in larger amounts in the majority of normal female subjects.

Twenty-seven subjects with various endocrine disorders were also studied. The results are tabulated in Table II.

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Establishment of Lymphoid Cell Lines in Patients With Common Viral Diseases

IRVING M. PALTROWITZ, M.D., YASHAR HIRSHAUT, M.D.,
PETER PAPENHAUSEN, B.A., WALTER HENLEY, M.D.,
KURT HIRSCHHORN, M.D., AND
PHILIP R. GLADE, M.D.

Introduction

Recent findings have shown that circulating lymphocytes from patients with a variety of neoplastic diseases such as leukemia and Hodgkin's lymphoma (1, 2), presumed viral diseases such as infectious mononucleosis and hepatitis (3–6), and normal individuals (7) have potential for long-term in vitro proliferation in suspension culture. A herpes-like virus (HLV, Epstein-Barr virus) has been found in these cultured cells of Burkitt's lymphoma (8), infectious mononucleosis (9), and hepatitis (10), and some investigators have suggested this virus may be responsible for the long-term in vitro proliferative potential (11, 12). A common denominator in these disorders is the presence in the peripheral circulation of increased numbers of atypical lymphocytes which incorporate radioactively labeled DNA precursor (13, 14), suggesting that these cells are in spontaneous proliferation in vivo.

The present studies were undertaken to determine if peripheral blood lymphocytes from patients with well-defined viral disorders associated with an atypical lymphocytosis, such as mumps, measles, varicella, herpes zoster, and herpes simplex show a similar potential for long-term in vitro proliferation. The association of HLV was investigated in these patients in an attempt to assess the significance of this agent in the establishment of long-term lymphoid suspension cultures.

Materials and Methods

Patients with well-defined clinical manifestations of mumps, measles, varicella, herpes zoster, and herpes simplex were obtained from The Mount Sinai Hospital pediatric and ophthalmologic services from September 1968 to November 1969. Healthy age-matched controls were studied collaterally.

Preparation of Blood Slides

Differential white blood cell counts were performed on freshly prepared blood smears stained with Giemsa. DNA synthesis was measured by an autoradiographic technique previously described (15). Tritiated thymidine (specific activity 3.6 μc/mM, Schwarz BioResearch, Inc.) was added to 0.5 ml heparinized peripheral blood to a final concentration of 10.0 μc/ml whole blood and incu-

From the Department of Pediatrics and the Department of Ophthalmology, Mount Sinai School of Medicine of The City University of New York, N. Y. 10029, and the Sloan-Kettering Institute for Cancer Research, New York, N. Y. 10021.

bated at 37°C for two hours with intermittent shaking. The cells were then washed three times with 0.01M phosphate buffered saline at pH 7.4 and resuspended in the fetal calf serum. Smears were made on gelatin-coated slides, and fixed in absolute methanol for ten minutes. The slides were coated with NTB-3 Kodak emulsion at 43°C and placed in light-proof boxes containing desiccant for seven days. Slides were developed in D-19 Kodak developer, water, and Kodak fixer for three minutes each, and were washed in running water for 20 minutes. The autoradiographs were passed through successive solutions of 1.) 50% methyl alcohol and 50% citrate phosphate buffer, 2.) citrate phosphate buffer, and 3.) absolute methyl alcohol for three minutes, and then stained with Giemsa. One thousand mononuclear cells were analyzed and cells with ten or more grains above background were considered positively labeled.

Preparations of Cultures

Leukocyte cultures were prepared by gravity sedimentation of 10 to 20 ml heparinized peripheral blood (100 units non-phenol heparin per ml whole blood) at 37°C for one to two hours and centrifugation of the plasma supernatant at 250 × g at 20°C for 20 minutes. Aliquots of $9.0 \times 10^6 - 4.0 \times 10^7$ mononuclear cells (determined by direct differential count on a hemocytometer) were cultured at 37°C in 30 ml screwtop plastic prescription bottles containing 10 ml of RPMI 1640 medium (7) supplemented with 20% heat-inactivated fetal calf serum, penicillin, streptomycin, and 1-glutamine. Thirty percent of the supernatant culture fluid was removed weekly and replenished with fresh medium after gravity sedimentation of cells. No effort was made to maintain cell concentrations. Cultures were observed daily for characteristic acid pH changes in the medium and were examined with a Zeiss inverted microscope for signs of proliferation, i.e. free-floating clumps of cells and increase in cell number. Cells growing in long-term culture were maintained by splitting the cultures and replenishing medium twice weekly as above.

Determination of Antibody

Anti-HLV antibody titers were assayed by standard indirect immunofluorescent techniques (16) utilizing the HLV-rich Jijoye (G) Burkitt lymphoma cell line as target cell and a fluorescein-conjugated goat anti-human IgG. Titers greater than 1:10 serum dilution were considered positive. Presence of HLV was detected in cell lines by direct immunofluorescence.

Results

Thirty-eight patients with clinically diagnosed measles, mumps, varicella, herpes zoster, and herpes simplex, and 13 control patients were studied (Table I). Patients with viral illness had a differential count of between 8% and 83% lymphocytes in their peripheral blood smears with a mean of 38% and a median of 36%. The control group ranged from 10% to 90% and had a mean of 46% with a median of 45%. Patients with infection had an atypical lymphocytosis

TABLE I

Characteristics of Peripheral Lymphocytes from Patients Studied

Diagnosis	Number of Patients	Number of Lymphocytes per 100 White Cells	Number of Atypical Lymphocytes per 100 Lymphocytes	Percent of Lymphocytes in DNA Synthesis
Normal	13	Range 10–90	Range 1–43	Range 0.0–1.0
		Mean 46	Mean 19	Mean 0.36
		Median 45	Median 10	Median 0.35
Viral disease	36	Range 8–83	Range 4–100	Range 0.0–6.0
		Mean 38.3	Mean 36.5	Mean 1.5
		Median 36.0	Median 33	Median 0.7
Mumps	3	Range 11–61	Range 30–50	Range 0.4–4.6
		Mean 34	Mean 40	Mean 2.7
		Median 30	Median 30	Median 1.5
Measles	10	Range 10–70	Range 10–45	Range 0.4–6.0
		Mean 38.1	Mean 28.5	Mean 1.95
		Median 37	Median 29	Median 1.20
Varicella	6	Range 20–83	Range 4–72	Range 0.2–4.8
		Mean 48.6	Mean 34.5	Mean 1.9
		Median 50	Median 23	Median 0.7
Herpes simplex	10	Range 16–77	Range 16–73	Range 0.0–1.6
		Mean 38.3	Mean 32.6	Mean 0.64
		Median 35	Median 28.0	Median 0.30
Herpes zoster	6	Range 8–59	Range 30–100	Range 0.1–3.6
		Mean 33	Mean 57	Mean 1.0
		Median 30	Median 46	Median 0.5

TABLE II

Continuous Cultures from Viral Diseases

Diagnosis	No. Patients	No. Specimens	Continuous Cultures
Normal	13	24	0
Mumps	3	3	1
Measles	10	10	3
Varicella	6	6	0
Herpes zoster	6	6	3
Herpes simplex	12	12	3

ranging from 45% to 100% of their lymphocytes with a mean of 36% and a median of 33% compared to a mean of 19% and a median of 10% in controls. The patients with viral diseases had, on the average, a lymphocyte count slightly lower than the control population. The percent of lymphocytes in DNA synthesis was higher in each infection group compared to the control group.

Suspension Cultures

Long-term suspension cultures were obtained from ten of the 38 patients with viral disorders (Table II). The cultures were established from patients with mumps, measles, herpes zoster, and herpes simplex, but attempts were unsuc-

TABLE III

Comparison of Peripheral Lymphocyte Characteristics Yielding Successful or Unsuccessful Cultures

	Unsuccessful Cultures	Established Cultures
Number of Lymphocytes per 100 White Cells	Range 8–70 Mean 25.7	Range 21–83 Mean 26.1
Number of Atypical Lymphocytes per 100 Lymphocytes	Range 4–100 Mean 26.7	Range 20–73 Mean 29.0
Number of Lymphocytes in DNA Synthesis	Range 0.0–6.0 Mean 0.56	Range 0.1–1.6 Mean 0.13
Lymphocytes Cultured	Range $9.0 \times 10^6 - 3.0 \times 10^7$ Mean 2.0×10^7	Range $1.0 \times 10^7 - 2.8 \times 10^7$ Mean 1.8×10^7

TABLE IV

Cell Lines Derived from Patients with Viral Induced Lymphoproliferative States

Cell Line	Disease	HLV Antibody	HLV in Cell Line (Antigen)
PGIP-3	Mumps	1:640	Negative
PGIP-4	Herpes zoster	1:640	Negative
PGIP-6	Measles	1:40	Negative
PGIP-7	Herpes simplex	Negative	Positive
PGIP-8	Herpes zoster	1:160	Positive
PGIP-9	Herpes zoster	1:160	Positive
PGIP-12	Herpes simplex	Negative	Positive
PGIP-40	Measles	1:160	Negative
PGIP-45	Herpes simplex	Negative	Positive

cessful from the six patients with varicella. The continuous proliferation, as evidenced by increased acidity of the medium and increased clumping of cells in suspension, were noted by 34 to 60 days. No long-term lines were established from control patients. Absence of lymphoid cells in control cultures was noted by 30 to 73 days. Under light microscopy the cells in long-term culture appeared lymphoid in character with a spectrum of cell types from small, mature-appearing lymphocytes to cells lymphoblastic in size and morphology. The doubling time of the cultures ranged from 48 to 72 hours. By analysis of the number of lymphocytes, atypical lymphocytes, and lymphocytes in DNA synthesis from the peripheral blood specimens, it was not possible to predict which patient would have cells establishing long-term lines (Table III).

Eighteen out of 32 patients had anti-HLV antibody in their initial sera. Titers in these patients were from 1:10 to 1:640. In five out of nine long-term lines studied to date, HLV antigen were demonstrated by immunofluorescent staining (Table IV). It is interesting to note that of the 14 patients who had no detectable anti-HLV antibody by immunofluorescence in their sera, three patients with herpes simplex established continuous cell lines. HLV antigen was present in these same cell lines.

Discussion

A variety of immunologic and nonimmunologic stimuli have been shown to initiate in vitro a series of morphological alterations in small lymphocytes associated with new DNA and RNA synthesis leading to mitosis and cell division (17). This process, termed lymphocyte transformation, has confirmed that the lymphocyte, rather than an end stage cell, is a resting cell capable of further differentiation and proliferation. Of particular interest is the striking similarity of these transformed cells to the atypical lymphocytes in peripheral blood of patients with a wide variety of infectious, lymphoproliferative, and immunogenic disorders. These observations suggest that lymphoid cells in the peripheral circulation in patients with an atypical lymphocytosis are undergoing spontaneous differentiation and proliferation.

Moore and his coworkers (7) have shown that circulating lymphoid cells from most individuals can be established in long-term culture. These attempts usually require large quantities of cells and maintenance of optimal cell concentration. This suggests that cells with a proliferative potential exist in all normal individuals in low concentrations. Similar long-term suspension cultures have been established from peripheral blood lymphocytes of patients with lymphoblastic leukemia (1), lymphosarcoma, Hodgkin's lymphoma, and multiple myeloma (2). Using small aliquots of blood, long-term lymphoid suspension cultures have been established from patients with infectious mononucleosis (4) and viral hepatitis (5). With these techniques long-term cultures were not obtained from normal patients, suggesting that this method is selective for those conditions which have a proliferative potential above the normal range and that there is an increased proliferative potential in patients with presumed viral disorders associated with an atypical lymphocytosis. Our present studies with mumps, measles, herpes zoster, and herpes simplex have demonstrated that known viral diseases with atypical lymphocytosis have a similar potential for long-term culture above the normal range. Although the number of patients studied was small, it can be seen that between 25 to 30 percent of peripheral blood lymphocyte samples from these patients with viral diseases will produce long-term cultures. This correlated with the results obtained from the previous studies with infectious mononucleosis (18) and viral hepatitis (5). The increased uptake of H^3-thymidine by lymphocytes from viral disease patients compared to uptake by cells from control patients supports the evidence for increased proliferative potential of the lymphoid cells in vivo in these patients. Nearly all of these labeled cells are atypical lymphocytes (19). Why long-term cultures were not obtained from all of these patients remains unknown, but the answer to this question may lie in the methods of culture preparation. We are also unable to explain why no long-term lines were established from the varicella patients. This is of interest because antigenic and biologic identity of the virus responsible for varicella and herpes zoster (20) has led to a general acceptance that varicella and herpes zoster represent different manifestations of infection with a single viral serotype.

In repeated attempts to induce increased lymphoproliferative potential in vivo, by known virus, we were unable to obtain long-term cultures from nine patients given subcutaneous injections of live, attenuated measles vaccine (Lirugen®, Pitman-Moore) and from one patient given mumps vaccine (Lederle). Blood specimens were obtained on the day of inoculation and seven and ten days after inoculation. The apparent lack of increase of potential in these specimens may reflect the timing of the blood sampling, the immunizing dose, or the virus–cell relationship.

Studies with vaccinia immunization nevertheless demonstrate that this live viral stimulation will increase potential of circulating lymphocytes for long-term in vitro proliferation. Lines were established from three of 12 patients immunized. Preliminary attempts to induce lymphoproliferative potential in vitro with herpes virus were unsuccessful. (Herpes simplex virus No. 1539 and No. 1543 obtained from the laboratory of Dr. H. Hodes, Mount Sinai Hospital, were added to 10 ml RPMI 1640 medium containing 1.0×10^6 to 3.0×10^6 lymphocytes per ml in concentrations of 10^5 TID to 10^1 TID.) Attempts in our laboratory to produce in vitro an increased potential for long-term culture of lymphoid cells from patients without evidence of disease have been successful, however, using a purified phytohemagglutinin preparation in the stimulation of peripheral lymphocytes (21).

The role of infectious agents in the increased proliferative potential of circulating lymphocytes in these viral disorders as well as in infectious mononucleosis and viral hepatitis remains unknown (6). It would be of great interest to know if these events are caused by the etiological agent. Replication of virus within circulating lymphocytes has been established and seems to be increased in stimulated cells (22). The presence of disease specific virus in these lines is currently under study, but none has been found to date (23). Anti-HLV antibody and HLV antigen has been found in sera and cell lines from virtually all patients with Burkitt's lymphoma (24), carcinoma of the posterior nasopharynx (25), infectious mononucleosis (26), and sarcoidosis (27). The presence of antibody uniformly in sera from these patients has led to the suggestion that HLV is the etiologic agent for some of these diseases (26). Gerber further suggests that the agent is a prerequisite for long-term culture of lymphoid cells (12). We have carefully investigated serum from our patients with viral diseases and the cell lines derived from these patients for the presence of HLV antibody and antigen by immunofluorescence. Sera from most of our patients had positive titers of anti-HLV antibody, and many cell lines derived from these patients had demonstrable HLV antigen. Investigation of HLV in our patients with well-defined viral disease, however, has uncovered two additional provocative facts. Three patients with HLV antibody in their sera produced cell lines without HLV antigen, suggesting that the herpes-like virus may not be a prerequisite for long-term in vitro proliferation. These cell lines may have actually had viral antigen and lost it prior to the investigation. Of greater significance, three herpes simplex patients with no detectable anti-HLV antibody by standard screening tests produced long-term lymphoid cell lines containing HLV antigen. It must be noted that these sera were screened by immunofluorescence and the results should be checked by the complement fixation method, a more sensitive test. This data suggests that HLV may exist in a latent state in individuals without eliciting a detectable immunologic response. Perhaps all of us harbor this agent which may be congenitally acquired. It is quite possible that the ubiquitous HLV is a latent infection in the lymphoid stem cells, and that stimulation of the cells by other agents or antigens results in a concomitant replication of HLV. The increased production of HLV then may act as an immunologic booster for a secondary antibody response. The presence of anti-HLV antibody in patients with lymphoproliferative disorders of unknown etiology such as Burkitt's lymphoma and infectious mononucleosis need not, therefore, imply a causative role for this particular agent. Seroconversion may result from factors other than primary exposure to HLV. Careful follow up of HLV antibody negative individuals from whom it is possible to establish long-term cell lines harboring this agent should allow us to determine the significance of HLV in the etiology of lymphoproliferative disorders of unknown etiology.

Summary

Circulating lymphoid cells from patients with clinical viral diseases (mumps, measles, herpes zoster, herpes simplex) showed increased numbers of atypical lymphocytes which incorporate radioactively labeled DNA precursor and have potential for in vitro proliferation above the normal physiologic range manifested by establishment of long-term lymphoid cell lines. No disease specific virus has been found to date in the cell lines established.

Herpes-like virus (HLV, Epstein-Barr virus) has been demonstrated in many of the cell lines by immunofluorescence. Sera of most patients contained significant titers of anti-HLV antibody. In a small number of instances, patients who had no anti-HLV antibody by standard screening methods were found to have HLV antigen in their established cell lines. Also, some patients who had anti-HLV antibody in their sera produced long-term lymphoid lines with no demonstrable HLV antigen.

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Health Resources in East Harlem

COURTNEY B. WOOD, M.D., MARGARET C. OLENDZKI, PH.D., AND
CHARLES H. GOODRICH, M.D.

The first step towards improvement of health care in East Harlem is to assess the present system. For most isolated communities this is a relatively simple task almost ending at the point when an inventory has been taken of the various health facilities and personnel located in or near the area. In a community within a much larger complex of communities, the task of identifying the health resources serving the local population becomes much more complicated. Such is the problem as one looks at the health resources of East Harlem. It is apparently rather amply supplied with health care facilities within its geographic boundaries, at least in comparison with some other low-income areas; but the extent to which these serve the local population—still more, the adequacy with which they do so—is far more problematic.

Inpatient Facilities

General hospitals

There are four general hospitals in East Harlem—three voluntary and one municipal. They provided a total bed complement of 2,575 general care beds in 1968 (see Table I). In addition, Mount Sinai had 124 beds for mental illness; and Metropolitan had 100 beds for mental illness, plus 105 for tuberculosis, and 20 for long-term care. Manhattan State on Ward's Island is a 3,238-bed mental hospital.

Information on the areas served by specific hospitals is scanty, but some clues may be pieced together from different sources, mostly unpublished. Special studies of Metropolitan Hospital's patient population have recently been conducted or compiled from existing sources by the architectural firm of Russo and Sonder, as part of the planning for the future of the hospital. Table II utilizes some data compiled for their report (1). The official hospital district is a large one, extending from 42nd Street to 116th Street, and from river to river. But more than half the inpatients come from the northeast corner of the Service Area, namely, East Harlem. Not too many inpatients come from the West Side, and very few from the wealthy section of the East Side below East Harlem. Metropolitan Hospital, then, does to a considerable extent seem to serve the needs for hospitalization of East Harlem residents.

This is far less true of the voluntary hospitals located in East Harlem. A specialty hospital like the Hospital for Joint Diseases, presumably draws from a rather wide catchment area, rather than serves only its own community. The fact that Flower and Fifth Avenue Hospital has only 85 ward beds out of its 406 beds suggests the limitations of its service to East Harlem. And Mount Sinai's diffusion of inpatient population throughout New York City can be

TABLE I

General Hospital Beds in East Harlem in 1968

Hospital	Medical Surgical	Pediatric	Maternity	Total
Mount Sinai	852	134	95	1,081
Metropolitan	524	160	74	758
Flower and Fifth Avenue	306	43	57	406
Joint Diseases	289	41	—	330
Total	1,971	378	226	2,575

TABLE II

*Patients Admitted to Metropolitan Hospital in 1968, by Health District and Health Area**
(Projected N = 15,885)

Area of Residence	Percent of Patients	
East Harlem		54.4
north (Health Areas 16, 17)	4.1	
north central (20, 21)	15.4	
east central (25, 28, 10)	10.0	
west central (26)	13.4	
south (28, 20, 33)	11.5	
Central Harlem		8.9
Riverside		12.6
Kips Bay & Yorkville		4.7
Other Manhattan		7.1
Outside Manhattan		12.3
Total		100.0

* Special study by Russo & Sonder, derived from New York City Department of Hospitals, Bureau of Medical Statistics, 1968 Inpatient Origin & Characteristics Study Data. See Report, pp 52–8.

documented statistically. A study of a sample of medical records in 1967 (2) showed only about 12 percent of inpatients living in East Harlem (Table III).

To what extent are East Harlem residents admitted to hospitals outside that geographic area? Here the evidence is still more sketchy. Harlem Hospital and the New York Hospital are the largest hospitals near but outside the boundaries of East Harlem. There is no evidence to suggest that they supply a great deal of care to East Harlem residents. The continuing Harlem Community Health Survey conducted by Harlem Hospital's Department of Patient Care and Program Evaluation, which includes the northern part of East Harlem down as far as 110th Street, reports "relatively little" use of Harlem Hospital by East Harlem residents compared to those of Central Harlem (3). The New York Hospital-Cornell Project found welfare recipients living on the east side of Manhattan, including East Harlem from 96th to 106th Streets, to be rela-

TABLE III

Inpatients Seen at The Mount Sinai Hospital in 1967, by Area of Residence
(n = 1,011)

Area of Residence	Percent of Patients	
Manhattan		44
northeast (East Harlem)	12	
southeast (south of East 96th St.)	12	
northwest (north of West 92nd St.)	11	
southwest (south of West 91st St.)	10	
The Bronx		18
Queens		12
Brooklyn		9
Staten Island		1
Outside New York City		16
Total		100

tively unfamiliar with the New York Hospital and unlikely to have used it; Puerto Ricans were especially unlikely to have been there (4).

It seems probable that the people of East Harlem are occasionally admitted to a large variety of different hospitals, mainly voluntary, scattered over the city, but that no one single hospital outside East Harlem supplies a great deal of their inpatient care. This hypothesis will be tested in the survey of East Harlem shortly to be carried out by the Mount Sinai Department of Community Medicine.

Nursing homes and infirmaries

Within the boundaries we have designated as East Harlem there are two extended-care facilities in addition to the hospitals. The Florence Nightingale Nursing Home is a proprietary institution with 407 beds; the Home and Hospital of the Daughters of Israel is a voluntary home for the aged with 142 beds. Neither of them is particularly likely to serve East Harlem residents predominantly. Located on the sourthern edge of East Harlem, the nursing home probably draws more from the area immediately south than to the north; while the home for the aged, under religious auspices, probably draws patients of that faith from a wide area.

The New York Hospital-Cornell Project cited above found that welfare recipients originally living on the east side of Manhattan, when in need of nursing home care, would be admitted to a very large number of different nursing homes all over Manhattan and beyond (5). Even when efforts were made to concentrate them in one or two homes, the shortage of nursing home beds made this very difficult: a vacancy had to be accepted wherever it could be found. This must surely contribute to the isolation of elderly patients who, after many years of living in a community such as East Harlem, must finally be institutionalized far from any remaining family or friends.

Addiction service agencies

Following is a list of agencies located in the East Harlem Community which provide services in the field of addiction (data extracted from Narcotics Services Directory of Human Resources Administration, March 1970).

Agency	*Service Provided*
1. Community Narcotics Education Center	Prevention education
2. Corps Outreach Program of Salvation Army	Residential and nonresidential treatment and rehabilitation
3. Division of Community Mental Health	Prevention education and residential treatment and rehabilitation
4. East Harlem Phoenix Center and House	Prevention education, resident and nonresident treatment and rehabilitation
5. East Harlem Youth Corps	Prevention education and nonresident treatment and rehabilitation
6. Exodus House	Resident and nonresident treatment and rehabilitation
7. Harlem Span C.D.C.	Prevention education and nonresident treatment and rehabilitation
8. 2 Harlem Hospital OPD Satellites	Nonresident treatment and methadone
9. Help Addicts Voluntary; also, Haven, Inc.	Nonresident treatment and rehabilitation
10. Lower East Harlem Satellite	Prevention education
11. Metropolitan Hospital Center	Residential treatment and rehabilitation
12. Mount Sinai Hospital	Residential and nonresidential treatment and rehabilitation and methadone
13. Odyssey House	Prevention education, resident treatment and rehabilitation
14. Region III MCDA	Job training and placement

The extent to which the above listed agencies are involved in care of East Harlem residents has not been determined, but the wide variety of agencies involved in addiction services immediately raises questions as to whether these various agencies are in communication with each other and whether their efforts in the field fit into an overall plan of attack on this very difficult and complex problem. Further study of this phase of health resources should be explored in depth at some future date.

Ambulant Care Facilities

Outpatient clinics and emergency rooms

By far the largest number of doctor—patient contacts in East Harlem occur in the hospital setting. Table IV shows the number of patient visits made in 1968 to hospitals in the East Harlem area. If these close to one million visits were indeed made by the 180,000 inhabitants of East Harlem, this would average nearly five visits per person for this source of care alone. Clearly some patients from other areas attend the hospitals in East Harlem, although there is reason to believe this happens far less with ambulatory care than with inpatient care. Common sense would dictate, and studies have confirmed, that patients

TABLE IV

Patient Visits to Hospitals in East Harlem in 1968

Hospital	OPD Visits	ER Visits	Total Visits
Metropolitan	356,450	91,558	448,008
Mount Sinai	176,392	93,702	270,094
Joint Diseases	59,997	18,098	78,095
Flower Fifth	10,891	19,645	30,536
Total	603,730	223,003	826,733

TABLE V

Metropolitan Hospital Outpatients, 1966, by Health District and Health Area*
(Projected N = 141,000)

Area of Residence	Percent of Patients	
East Harlem		59.5
north (health areas 16, 17)	2.7	
north central (20, 21)	17.2	
east central (25, 28, 10)	13.3	
west central (26)	20.4	
south (28, 20, 33)	5.9	
Central Harlem		9.2
Riverside		16.0
Kips Bay & Yorkville		3.5
Other Manhattan		6.5
Outside Manhattan		5.3
Total		100.0

* Excludes patients using emergency room only. Based on data derived from Raymond C. Lerner, "New York City Municipal Hospital Outpatient Population Study Data," 1966.

travel least far for emergency care, somewhat further for clinic care, and, if private patients are included, furthest of all for hospitalization (6). The system of admission to the hospital where one's physician has staff privileges diffuses geographically the inpatient population of any given hospital, and so does the factor of referral of challenging cases to the teaching hospital. Both these factors operate in East Harlem's voluntary hospitals.

The pattern of use of Metropolitan Hospital by its outpatients is similar to that shown for its inpatients in Table II. The same report cited above estimates that in 1966 approximately 141,000 outpatients made a total of 427,000 visits to Metropolitan Hospital (7). About 60 percent of these patients came from East Harlem (see Table V). It should be noted that this study did not include the emergency room: there may well be an even greater concentration of local residents among the users of Metropolitan's emergency room.

The Mount Sinai medical chart study referred to above showed 41 percent of OPD patients, and 51 percent of emergency room patients, seen in 1967 to be residents of East Harlem (8). The proportion of *visits* to Mount Sinai contributed by East Harlem people may well be higher than the proportion of patients, since clinic patients in general are more likely to make return visits if they are relatively close to their source of medical care than if they live far away (9).

If one had to hazard a guess, perhaps half a million hospital visits are made by East Harlem residents to the hospitals in their area. It is impossible to estimate the number of visits they make to other hospitals, the likeliest large ones being Harlem Hospital, the New York Hospital, and Lenox Hill: in the aggregate, these and the many smaller hospitals are unlikely to provide more than 100,000 visits between them. In addition, some care is provided by nonhospital clinics and some by private doctors.

Other clinics

The Department of Health is the chief supplier of out-of-hospital clinic services within the borders of East Harlem. Table VI summarizes broad categories of attendance at Health Department services in the East Harlem district. In its traditional role, however, the Health Department has stayed out of the direct provision of medical care; therefore, most of these services are for prevention or follow up rather than definitive treatment. This situation may shortly be changing.

Figure 1 shows the location of all the facilities described in this section.

Private practitioners

In the summer of 1968, students and Community Medicine staff compiled an inventory of physicians and others with offices listed in East Harlem. Sources of information were the medical directories, the telephone directory, and lists

TABLE VI

*Attendance at Health Department Services in East Harlem in 1968**

Type of Service	Attendance
Child Health	30,088
Other Attention to Children	25,143
Dental	13,126
Tuberculosis	12,021
Testing & Immunization	11,358
Social Hygiene	9,562
Prenatal & Family Planning	8,453
Elementary Schools	7,897
Adult Hygiene	4,167
Eye	2,722
Secondary Schools	1,733
Nurse Home Visits	1,551
Cardiac & Orthopedic	815
Total	128,636

* Extracted from Table 43—Bureau of Records & Statistics, New York City Department of Health, September 9, 1969.

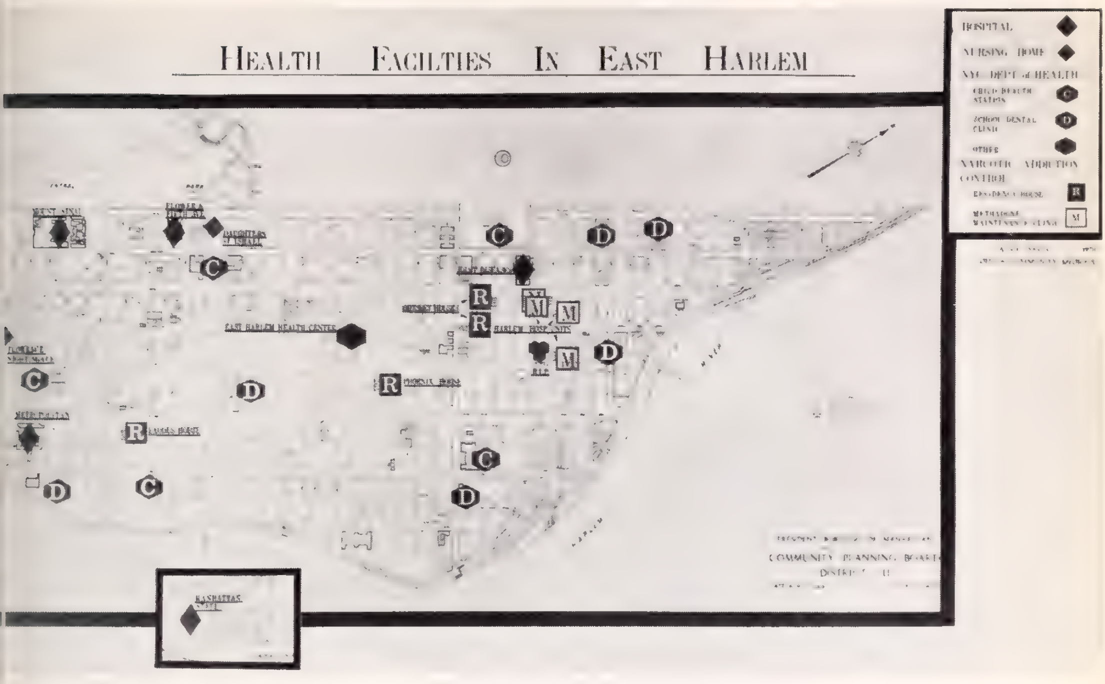
HEALTH FACILTIES IN EAST HARLEM
HOSPITAL
NURSING HOME
NYC DEPT of HEALTH
CHILD HEALTH STATION
SCHOOL DENTAL CLINIC
OTHER
NARCOTIC ADDICTION CONTROL
RESIDENCE HOUSE
METHADONE MAINTENANCE CLINIC
C
D
R
M
EAST HARLEM HEALTH CENTER
COMMUNITY PLANNING BOARD
DISTRICT 11

Fig. 1. Health Facilities in East Harlem.

compiled by other local health agencies. At that time there were 207 physicians with offices in the area. One hundred and forty were classified as specialists and 64 as general practitioners, with 12 of the latter having some specialty training. By far the largest number of specialists were psychiatrists (Table VII).

One hundred and fifty practicing physicians (excluding psychiatry, anesthesiology, and radiology) for a population of 180,000 persons would produce a physician-patient ratio of 1:1,200 which, when added to the hospital-based care reported above, could provide quite generously for East Harlem's medical care needs. But there is reason to suspect that rather few of these 150 physicians treat East Harlem patients to any great extent in their private practices. A study of their geographical distribution discloses a dense clustering around the two medical schools, New York Medical College and Mount Sinai. Relatively few are in the midst of the East Harlem community. There is a cluster of general practitioners located on both sides of 116th Street from Park Avenue to 1st Avenue. Many of these are elderly physicians who have long served the population of "Little Italy" which formerly predominated in this area and of which some vestiges remain. It is not known whether they now also serve the newer, Puerto Rican and black inhabitants of the surrounding area.

A few general practitioners, and one internist practicing general medicine are known to the staff of Mount Sinai and have extremely busy practices in the heart of El Barrio. But they are few in number, and should the hospitals ever decide to curtail their role in the primary care system of East Harlem, it is certain that private practice as presently available could not take their place.

TABLE VII

Field of Practice of Physicians with Offices in East Harlem, 1968

Field of Practice	Number of Physicians
General practice	64
Psychiatry	54
Surgery*	24
Internal medicine	19
Anesthesiology	12
Obstetrics-Gynecology	11
Pediatrics	9
Cardiology	2
Ophthalmology	2
Otolaryngology	2
Pathology	2
Dermatology	1
Neurology	1
Radiology	1
Not known	3
Total	207

* 17 general, 5 orthopedic, 2 neurosurgery

H.I.P.

The Yorkville Medical Group is one of the first medical group partnerships in New York City. It began to provide care for H.I.P. members on a capitation contract basis in 1947. It is now doing so for over 32,000 of H.I.P.'s 700,000 enrollees and is steadily growing. Fifty percent of this population is enrolled under Medicaid. The Yorkville group therefore provides under the same roof extensive medical care for persons of all socioeconomic levels. It has close ties with the community where it operates and, because a large proportion of the enrolled members live in East Harlem, it is now opening a peripheral center in a joint program with the East Harlem Tenants' Council. This new center is opening in June 1970.

Home health services

There is a wide variety of agencies which provide home health services to some residents of East Harlem. The volume of such services to the East Harlem population is not known, nor is the extent of need nor the gaps in service. There have been no recent studies in this community in this field, therefore, the following list is by no means complete:

1. Metropolitan Hospital operates a hospital-based organized Home Care Program.
2. Mount Sinai Hospital runs a hospital-based Blue Cross Home Care Service.
3. Voluntary nonprofit home health services include:

(a) The Visiting Nurse Service of New York which has a branch office in East Harlem in the district's Health Center
(b) The Little Sisters of the Assumption who serve East Harlem residents in the home
(c) The Dominican Sisters who operate a nursing home and home health aide service.

4. The Department of Health has public health nurses, operating out of the District Health Center, who visit and render services in the home.

5. Miscellaneous services in the home are provided or financed by:
(a) The Department of Social Services (homemaker service)
(b) Catholic Charities
(c) Childrens' Aid Society
(d) Community Service Society
(e) Special agencies such as the American Cancer Society.

Some of the other health professionals besides physicians whose offices are situated in East Harlem, many of which also group around the medical centers, include 45 dentists, 10 optometrists and 9 opticians, 5 podiatrists (there is also a College of Podiatry), 3 psychologists, and 3 chiropractors.

Some of the dentists and optometrists may well have come into East Harlem in response to Medicaid, and their numbers may have increased still further since these data were collected in 1968. However, the unpredictable ebb and flow of Medicaid financing may not contribute to a very stable supply of these needed services in the neighborhood.

There are about 36 pharmacies in East Harlem; of all the local health resources, they are the most evenly distributed throughout the area. How far the pharmacy serves as a health resource for the community, far beyond the filling of prescriptions and dispensing of nonlegend drugs for everyday complaints, is a question deserving of further study.

Discussion

On the face of it, geographic East Harlem is not lacking in health resources. Compared with some deprived areas of New York City, such as parts of Brooklyn, it is almost generously supplied. Yet, East Harlem is very far from having a satisfactory health care system. First, as we have tried to suggest from the meager evidence available, East Harlem is probably a "creditor" rather than a "debtor" medical care community: the health facilities geographically located here probably provide more service to non-East Harlem residents than East Harlem residents receive from the outside. This is to be expected in a community containing two medical schools, whose teaching centers attract referrals from all over the city and beyond, and whose medical staffs see their middle-class private patients from this base on the edge of the ghetto.

Second, and more seriously, the health resources that *are* available to East Harlem residents do not form a coherent health care system. A patient with tuberculosis may be seen in a voluntary hospital chest clinic, a city hospital chest clinic, or a Health Department chest clinic, with none of these three staffs communicating with other. The private physician in the ghetto cannot hospitalize his patients in any local hospital. The specialty and subspecialty expertise of the medical center is locked away from the community by an archaic system of clinic quotas and clinic hours that keep away the working man and woman. Meanwhile, the flood of patients with acute problems—making nearly a quarter of a million visits in East Harlem in 1968—jam into the cramped quarters of the emergency rooms.

The challenge confronting East Harlem, and all the health care resources within it, is how to bring some order and rationality and effectiveness into the nonsystem described above.

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Roentgen and Pathological Changes in the Gastrointestinal Tract in Herpes Zoster Generalizata:

A Unique Case and Brief Review

MANSHO T. KHILNANI, M.D. AND RHONA J. KELLER, M.D.

The following case of involvement of the gastrointestinal tract by herpes zoster, evidenced by roentgen examination and proved at autopsy, is presented as unique in the reported literature. A discussion of the findings and a brief review of relevant literature are added.

Case Report

A 61-year-old white woman, with polycythemia vera for 18 years, was admitted for pain in the inframammary region of the chest and epigastrium. The pain increased with inspiration. There was no cough, hemoptysis, or fever. Physical examination and x-ray examination of the chest just prior to admission were normal. The pain required frequent analgesics. The patient had developed anorexia and vomiting one day prior to admission. The polycythemia had been treated with P-32 and Busalfan® until three months prior to the present complaint. History of previous varicella was not ascertained.

Physical examination on admission showed the lips and nail beds to be ruddy. The chest was clear to percussion and auscultation. No lesions on the skin were evident. Slight abdominal guarding without rebound was noted in the epigastrium. The spleen was palpable one finger breadth below the costal margin.

Laboratory examination showed the hemoglobin to be 19.7 gm per 100 ml, RBC 5.8 million, and WBC 22,000 per ml. Urine showed a moderate albuminuria. Total bilirubin measured 1.5 mg per 100 ml, with direct 0.3 mg. Fasting blood sugar, BUN, electrolytes, amylase and SGOT were normal. Prothrombin time was 14 seconds (control, 12 seconds). Repeat films of the chest and abdomen were not remarkable. Phlebotomies reduced the hemoglobin to 14.6 gm per 100 ml. On the fourth hospital day, platelets were 254,000 per ml. Gallbladder examination was unsatisfactory. Because of unremitting epigastric pain, upper gastrointestinal examination was performed. Numerous discrete, sharply demarcated, round defects of uniform size were demonstrated in the distal half of the stomach (Fig. 1A, 1B, 1C). Similar defects were noted in the jejunum. The entire small bowel was dilated (Fig. 2). Patient remained afebrile although the abdominal and epigastric pain persisted. A few days after admission, vesicles of herpes zoster developed over the inframammary region of the chest. On the sixth hospital day, the temperature rose to 102°F and the patient became hypotensive. Later, distension of the lower abdomen developed. On vasopressor

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From the Department of Radiology, Mount Sinai School of Medicine of The City University of New York and The Mount Sinai Hospital, New York, N.Y. 10029.

drugs, intravenous fluids, and antibiotics, no clinical improvement was observed. Distention of the abdomen increased and the patient had several diarrheal bowel movements. Because of abdominal distention, tenderness, and rebound, a peritoneal tap was performed. It failed to yield any fluid. Examination of the chest showed infiltration in the left upper lobe. Isolated vesicles indistinguishable from varicella were observed on the chest and abdomen. Subsequently, icterus developed and bilirubin rose to 14 mg per 100 ml with 9 mg direct. The patient failed to respond to treatment and died on the tenth hospital day.

Autopsy performed 6 days after barium meal revealed two crops of vesicles, one located in the region of the 9th to 11th ribs and the other in the mid-

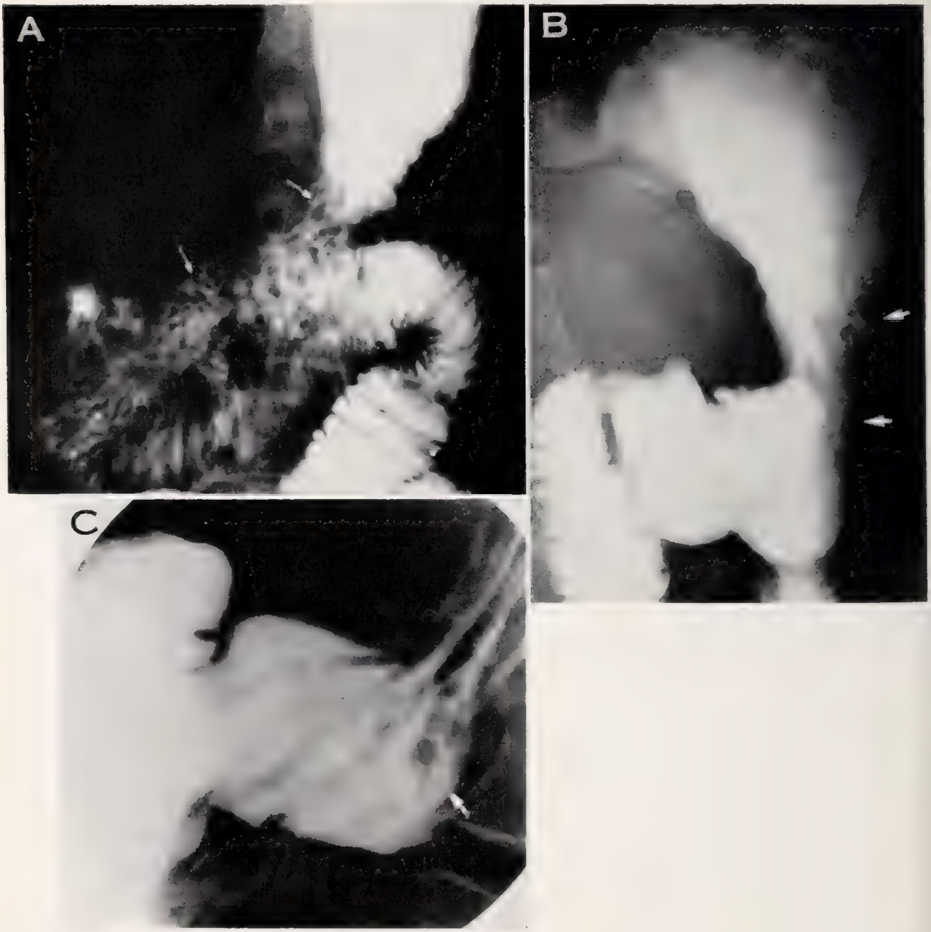

Fig. 1 A. Multiple round and oval defects, 3 to 5 mm, in diameter, are seen in the pars intermedia of the stomach. The defects are sharply outlined and discrete (arrows). B. The defects are seen in profile on the anterior wall (arrows). C. Spot view of the involved region outlines the discrete defects both on and in between the mucosal folds (arrows). Ulcerations are not evident.

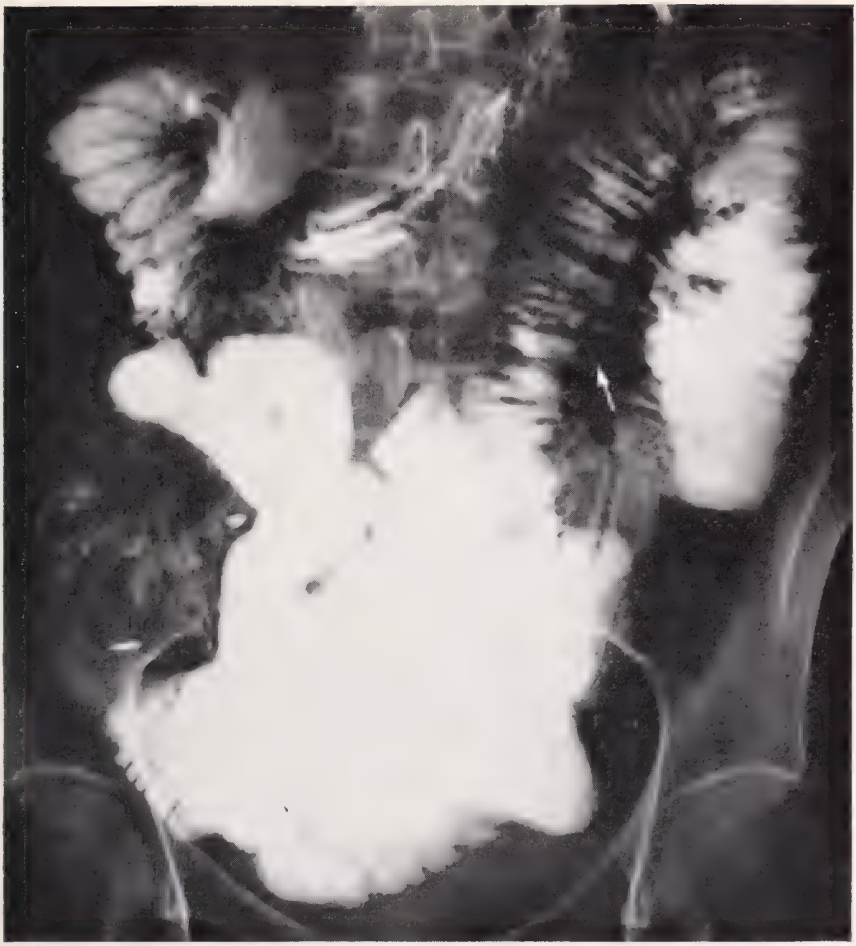

FIG. 2. One-hour examination shows dilatation of the small bowel. Numerous small round defects 2–3 mm in diameter are superimposed on the jejunal folds (arrows).

axillary region. The vesicles contained clear yellow fluid. Both crops of vesicles followed intercostal nerve distribution. Scattered over the entire thorax and abdomen were other vesicles, some of which contained hemorrhagic fluid. There was atelectasis of the right lower lobe and an area of consolidation in the left upper lobe. Pleural fluid or vesicles on the pleura were not seen. There was no pericardial effusion or pericardial vesicles. The liver was normal in size. The surface was mottled. An area of frank hemorrhage was seen inside the liver parenchyma. Intra- and extra-hepatic bile ducts and portal veins were unremarkable. The adrenals and pancreas showed areas of hemorrhage and necrosis. The spleen was enlarged. The esophagogastric junction and the stomach disclosed numerous circular ulcerations with hemorrhagic base, some up to 3 cm in greatest diameter (Fig. 3A). Similar hemorrhagic ulcerations were seen in the small bowel, primarily in the jejunum with a few scattered in the ileum and

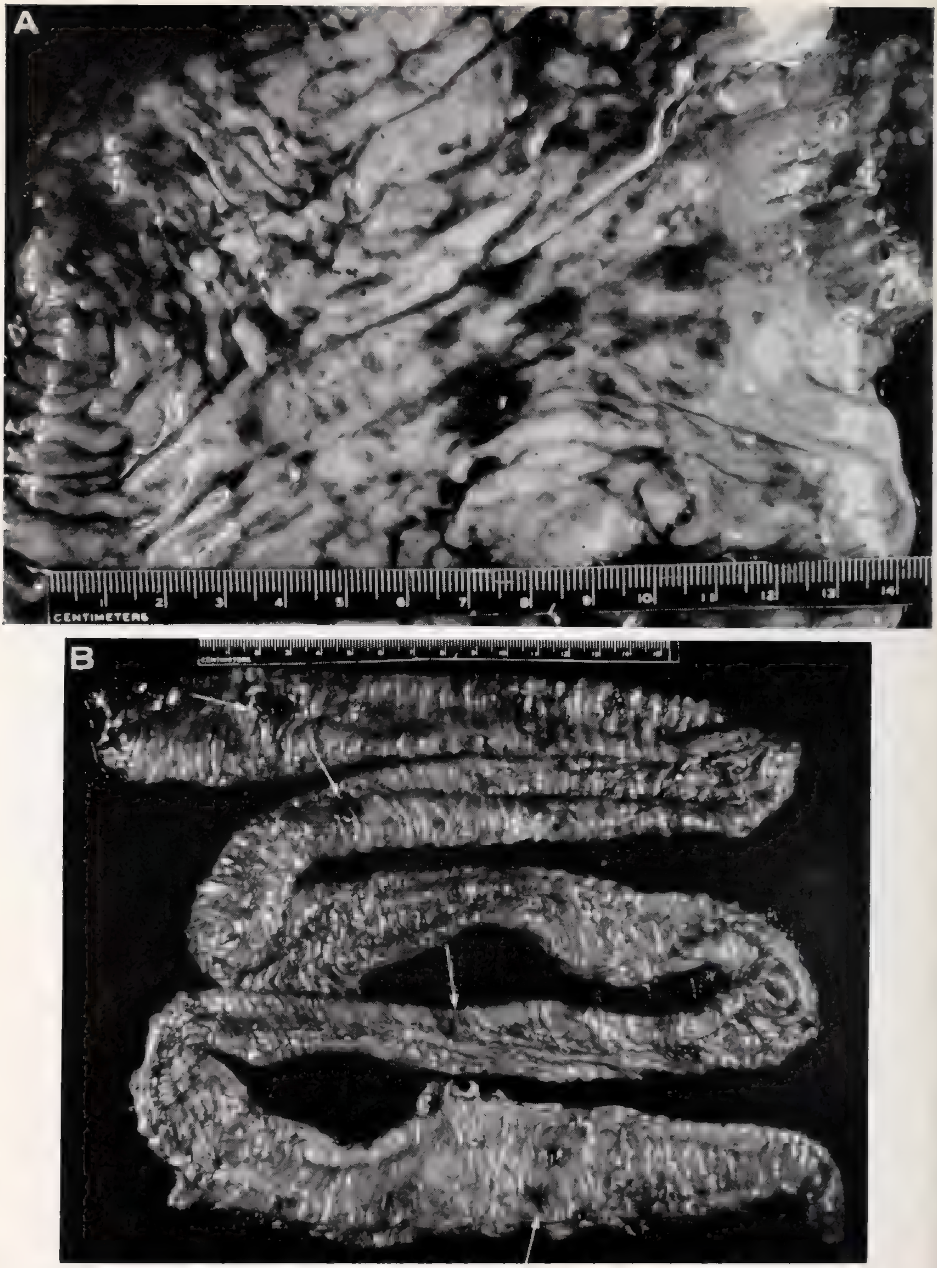

FIG. 3 A. At autopsy, the stomach, opened along the greater curvature, shows multiple discrete and ill-defined areas of ulceration with hemorrhagic bases. These correspond in location and size to the discrete defects demonstrated 6 days previously on the barium meal. B. An opened segment of upper jejunum shows multiple small ulcerations with hemorrhagic bases (arrows).

ascending colon (Fig. 3B). The entire small bowel was dilated; no perforation was seen. The serosa showed dilated vessels and scattered hemorrhagic ulcerations. The mesentery of the small bowel was edematous.

On microscopy, acute diffuse bronchopneumonia was diagnosed. Some alveolar and endothelial cells displayed intranuclear inclusion bodies. The esophagus revealed acute ulceration and inclusion bodies in inflammatory cells and in epithelial cells. Stomach, small intestine, and colon showed similar ulcerations and inclusion bodies in inflammatory and epithelial cells. Many ganglion cells in the myenteric plexuses of the intestinal wall contained intranuclear inclusion bodies.

The liver demonstrated diffuse areas of hepatic necrosis. There were intranuclear inclusion bodies in the hepatic cells, Kupffer cells and bile duct epithelium. Extensive necrosis and intranuclear inclusion bodies were also seen in the pancreas and adrenals. The intradermal vesicles were diagnostic of herpes zoster or chicken pox. Many of the epithelial cells in the vesicles displayed balloon and vesicular degeneration. These cells contained eosinophilic intranuclear inclusion bodies surrounded by a clear zone with margination of the nuclear chromatin.

The final anatomical diagnosis was polycythemia vera, generalized herpes zoster with involvement of the skin and viscera, specifically stomach, jejunum, ileum, and ascending colon, necrosis of the liver, pancreas and adrenals.

Discussion of Roentgen Aspects

The discrete nodular defects seen on barium meal study very likely were the vesicular stage of the varicella-zoster infection. These subsequently became ulcerated with hemorrhagic base. The role gastric and intestinal juices play in production of ulcerations is debatable. The assumption that the ulcerations were due to rupture of these vesicles is probably correct because of findings of intranuclear inclusion bodies in the inflammatory cells as well as in the epithelial cells. The hemorrhage was not due to purpura, occasionally seen in the viremic phase, as the prothrombin time and the platelets were normal. The defects of vesicles or ulcerations in the stomach and the intestine, however, are not specific as similar defects could be produced by coincidental polypoid mucosal folds or polyps in the stomach or multiple lymphomatous nodules.

There have been few roentgen studies in either segmental or generalized forms of herpes zoster. Scout films of the abdomen have shown non-specific adynamic ileus (8, 13). Twenty-five cases in the series reported by Gais et al (14) complained of abdominal pain, cramps, nausea and constipation. Physical examination revealed generalized or localized tenderness, and rigidity and melena were noted in two. Barium enema, gastrointestinal examination and gall bladder studies however were reported as unremarkable. To date, one case with changes on barium enema has been reported (13).

Herpes zoster in this case was segmental in distribution and the vesicles appeared over the distribution of the 8th and 9th thoracic nerves. A scout film of the abdomen obtained because of abdominal pain and distension suggested obstruction of the left colon. Barium enema showed a constricting lesion in the sigmoid with no retrograde obstruction, suggesting an inflammatory process or spastic colitis. Sigmoidoscopy performed later revealed no pathological condition up to 20 inches. Repeat barium enema study four days later showed marked improvement. The colon on a third examination one month later was normal. The diagnosis of involvement of a segment of the colon by herpes zoster virus was likely; but other possibilities such as ischemic colitis or diverticulitis cannot be completely excluded. Shirduan et al reported a case of generalized herpes zoster which, at autopsy, showed involvement of three discrete segments of distal ileum pathologically diagnosed as pseudo-membranous enteritis (23). They attributed these changes to zoster involvement of the lower dorsal spinal segments and the related ganglia of the autonomic nervous system rather than herpes zoster involvement of the ileum. They quote Hess et al who noted abnormal motility of the stomach in several cases with zoster involvement of D6 to D10 dermatomes. Roentgen findings, however, were not reported.

Because of the roentgen changes in the stomach and small bowel in our patient with polycythemia vera and generalized herpes zoster, the case is reported in some detail.

General Discussion

Herpes zoster, or shingles, and less often other viral exanthemata, are not uncommon complications in patients with neoplasm of the lymphoreticular system (2, 3, 4, 9, 11, 12). Rosenberg et al quote Williams who found herpes zoster in 2% of his 1733 patients (22). At this hospital, as many as one-third of the patients with lymphosarcoma, during the course of their disease, have been afflicted with this infection (8). The lowest recorded incidence of herpes zoster is 0.8%. The agent causing herpes zoster is antigenically identical with the varicella virus (6, 15, 16, 18, 24, 25, 26). Herpes zoster is believed to be a reactivation of latent varicella virus or possibly reinfection by the same virus (5). Unlike varicella, herpes zoster occurs in adults and is localized to one or more dermatomes. Generalization of herpes zoster is uncommon when no underlying lymphoma is present, probably because of antibody already present in the sera resulting from previous encounter (1, 6, 18). Herpes zoster becomes generalized more frequently when the infection occurs in the course of lymphoma, and low immunologic defences. The use of antimetabolites, alkylating agents and cortico-steriods may be predisposing factors (15). The generalization always follows initial segmental distribution, around the 5th day.

Rosenberg et al found involvement of one or more dermatomes in 64 of 1,269 cases of lymphoma reviewed, an incidence of close to 5% and only 4 out of these 64 became generalized (21). On the other hand, Craver and others state that the incidence of the generalized form is as high as 50% (9). The generalized form involves both the skin and the viscera. There have been several autopsy reports in the literature of visceral involvement during the course of herpes zoster-varicella viremia (7, 10, 14, 21) with and without associated lympho-reticular disease. Some of the reports have been in infants who died of varicella infection (20). Involvement of the gastrointestinal tract however was infrequent.

Summary

The diagnosis of gastrointestinal involvement should be strongly suspected when a patient with lymphoreticular neoplasia or a person receiving antimetabolites or alkylating agents develops generalized exanthemata and complains of abdominal symptoms of pain, guarding, or rigidity. Careful gastrointestinal study may then reveal the defects of vesicles or the resulting small mucosal ulcerations.

Acknowledgment

Our deep thanks are due to the Department of Pathology for providing slides and autopsy protocols in the preparation of this paper.

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Gardner's Syndrome: a Report of Four Cases

JULIUS J. LEICHTLING M.D.

More than 100 cases of multiple polyposis of the colon associated with hard and soft tissue tumors have been reported since Gardner and Richards established the hereditary pattern of this entity (1). The syndrome is inherited in a mendelian dominant pattern. Both sexes may transmit the disease. The colonic polyposis may be associated with one or all of the extraintestinal manifestations.

The following cases of two siblings and one child of each sibling are presented.

Case 1

A 44-year-old white male was admitted to The Mount Sinai Hospital on November 28, 1969. Ten months prior to admission his dentist noted osteomas of the patient's skull and mandible; a barium enema was advised. The patient had had four to six semiformed stools, containing considerable mucus, daily for the past several years. He complained of fatigue and weakness for the past several months. Examination revealed several osteomas of the skull together with a subcutaneous fibrotic mass of the left forearm (Fig. 1). A barium enema revealed multiple polyps throughout the colon and a large polypoid mass in the distal transverse colon (Figs. 2, 3). A skeletal survey demonstrated osteomas of the skull, right mandible, and left frontal sinus; osteomas of the right femur, fibula, and radius were also noted (Fig. 4). The remainder of the physical examination was not remarkable. The hemoglobin was 7 gm%. Approximately 70 polyps, ranging in size from 3 mm to 2 cm were fulgurated sigmoidoscopically prior to admission. Biopsies of two of the larger polyps were reported as benign adenomas.

On December 3, 1969, after several transfusions and bowel sterilization, a total colectomy and ileorectal anastomosis was performed 7.5 inches from the anus. The colon specimen demonstrated innumerable polyps throughout the large intestine (Fig. 5). When discharged from the hospital 13 days after the operation he was having four semiformed stools a day. He was sigmoidoscoped on two occasions postoperatively; four small polyps were fulgurated the first visit and six small polyps were fulgurated on February 19, 1971. His hemoglobin level remained normal and he had no complaints. His three children, two females, age 16 and 14 years, and one male, age 5½ years, were sigmoidoscoped and barium enemas were performed. No polyps were seen.

From the Department of Surgery, Mount Sinai School of Medicine, The Mount Sinai Hospital, and Mount Sinai Services at Elmhurst Hospital. Presented at the Clinical Congress of The American College of Surgeons, Chicago, October 12–16, 1970, and at the convention of The American College of Gastroenterology, October 26–28, New York City.

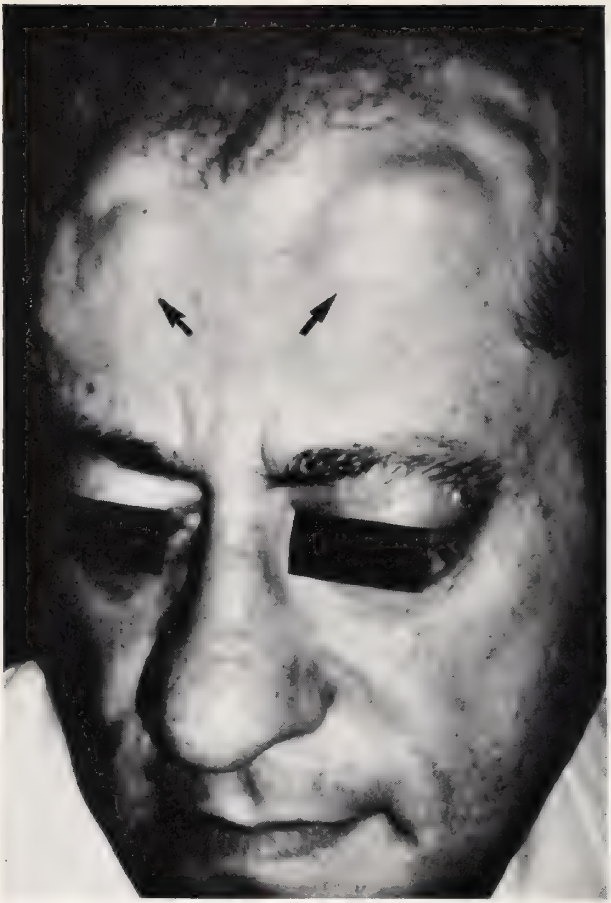

FIG. 1. Osteomas of skull, Case 1.

Case 2

A 36-year-old white, female, sister of Case 1, was examined in December, 1969. Her past history included the removal of numerous sebaceous cysts of the shoulders, back, abdomen, and vulva since she was 6 years old. A large osteoma was excised from the left iliac crest in 1958. A desmoid tumor involving almost the entire left anterior abdominal wall was resected in 1959.

The patient had no complaints. She had one formed bowel movement a day. Examination revealed osteomas of the skull, multiple sebaceous cysts and operative scars of the back, and an eleven-inch incisional scar of the left anterior abdominal wall with an incisional hernia of the lower third. There were also several sebaceous cysts of the pubic area and bilateral symmetrical cysts of the forearms (Figs. 6, 7a).

A barium enema exhibited two long pedunculated polyps of the splenic flexure; several other small filling defects were noted but could not definitely be interpreted as polyps. A skeletal survey revealed osteomas of the skull,

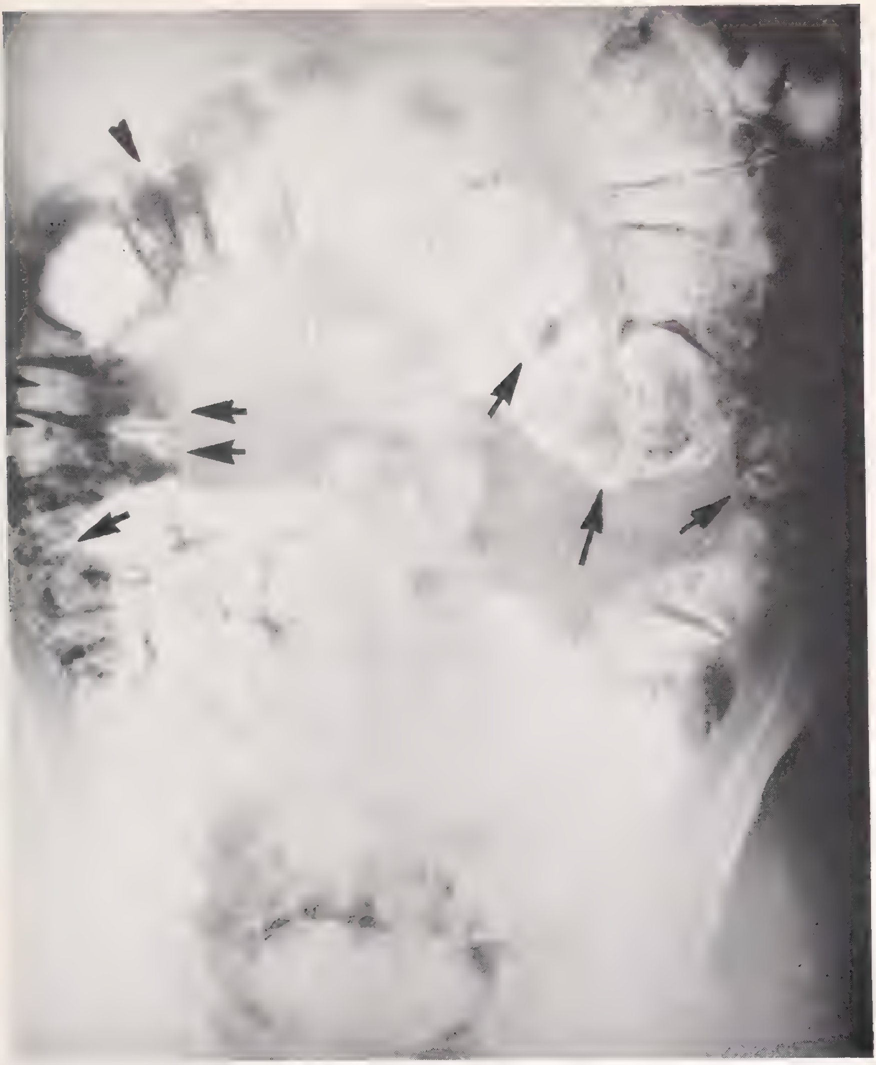

FIG. 2. Barium enema shows diffuse polyposis of the colon. Many polyps are readily identified (arrows). In other areas, masses of innumerable polyps exhibit a reticular pattern resembling fecal material. Case 1.

mandible, sinuses, eighth rib, and femur (Fig. 8). The patient delayed her consent for surgery for one year. Prior to her admission to The Mount Sinai Hospital seventeen rectal polyps up to one centimeter in diameter were sigmoidoscopically fulgurated.

On November 16, 1970, a total colectomy with end to end ileorectal anastomosis was performed 7 inches from the anal margin. Five recurrent fibromatous (desmoid) masses, up to 1½ inches in diameter, were excised from the abdominal wall in the area near the old left paramedian scar. In addition to the two polyps demonstrated in the barium enema, the colon specimen con-

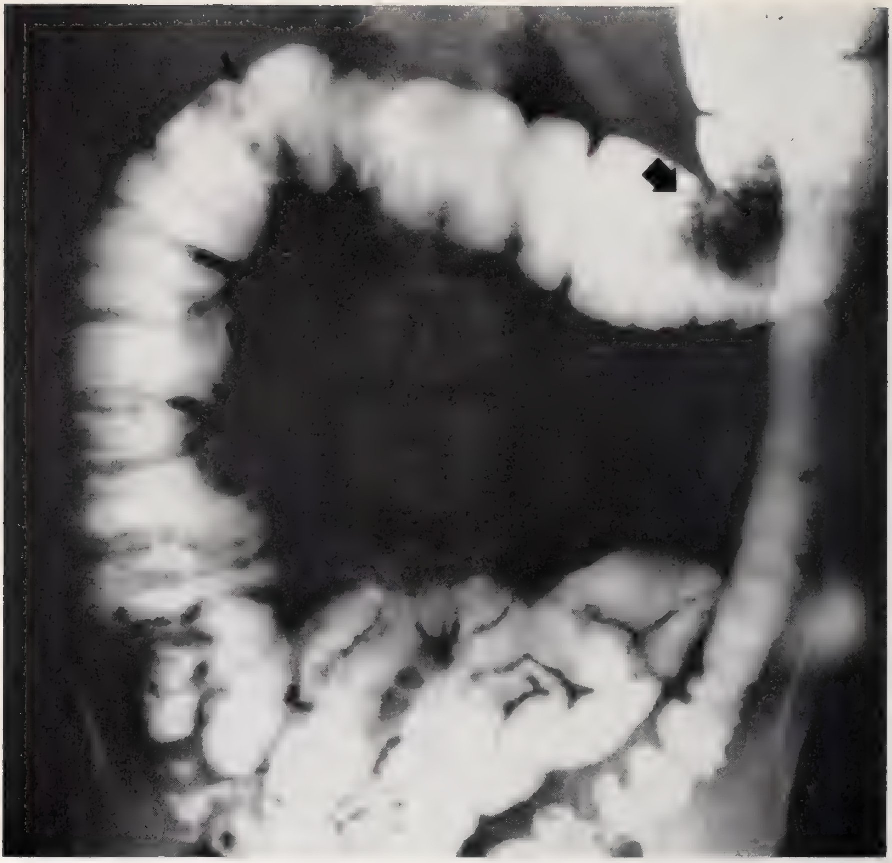

Fig. 3. Barium enema before evacuation and air instillation. Only a few polyps are noted together with the large adenoma of the distal transverse colon. Case 1.

tained 60 polyps situated mostly in the cecum, appendix, and transverse colon. At the time of her discharge, 10 days after the operation, the patient was passing 3 to 4 pasty stools a day. When last examined in February, 1971 she was in good health. Sigmoidoscopy was performed and four small polyps were fulgurated.

Case 3

A 16-year-old female, daughter of Case 2, was examined in December, 1969. She had no symptoms. The physical examination was unremarkable except for one osteoma of the frontal skull and two sebaceous cysts of the scalp (Figs. 7b, 9). Sigmoidoscopy revealed many tiny polyps 2 or 3 millimeters in diameter. The patient did not wish to have a barium enema performed.

The parents stated that the osteoma of the skull was present at birth; a photograph which was taken at the age of 6 months demonstrated the osteoma (Fig. 10).

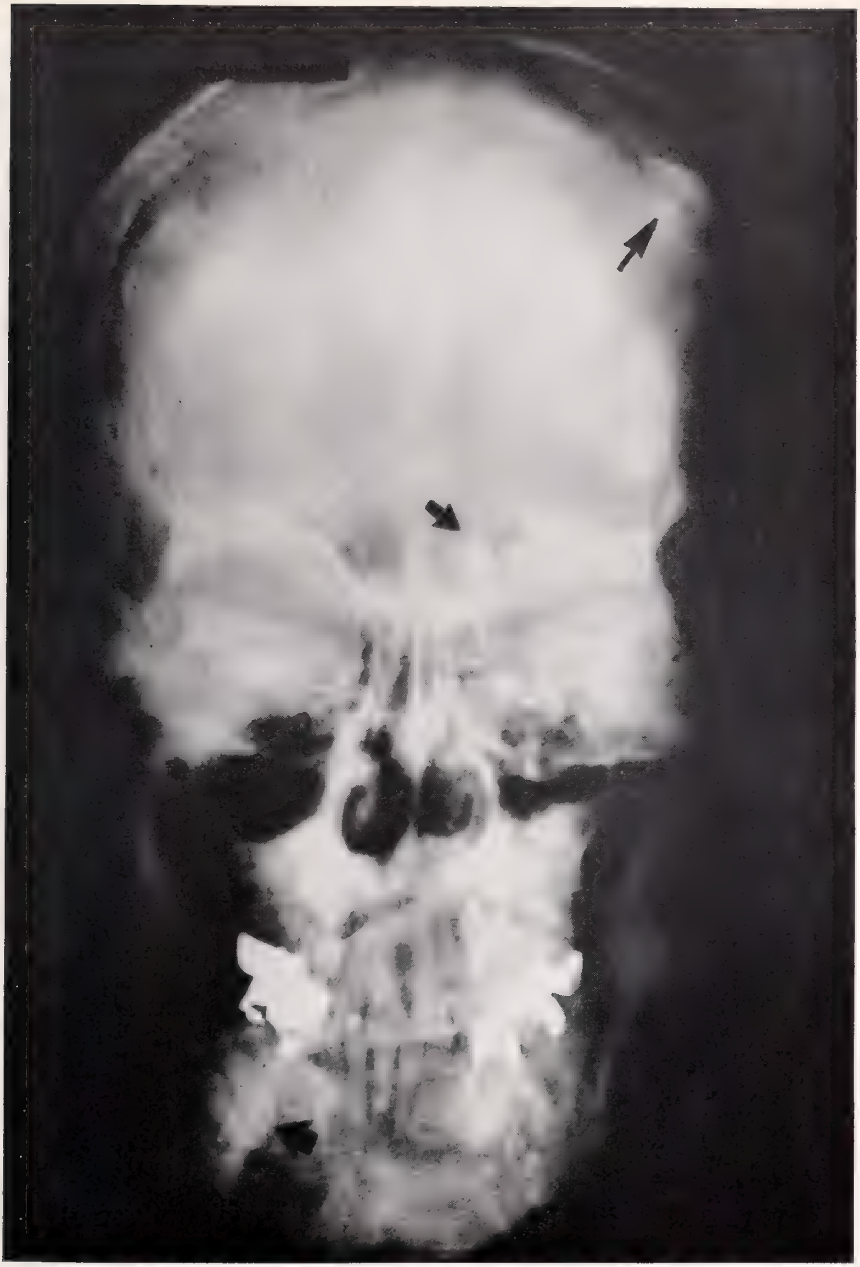

FIG. 4. Osteomas of the skull, mandible and sinuses. Case 1.

Case 4

A 14½-year-old female, daughter of Case 1, was examined in December, 1969. She was asymptomatic. One osteoma of the left frontal skull was noted. The examination was otherwise normal. A dental x-ray revealed several un-

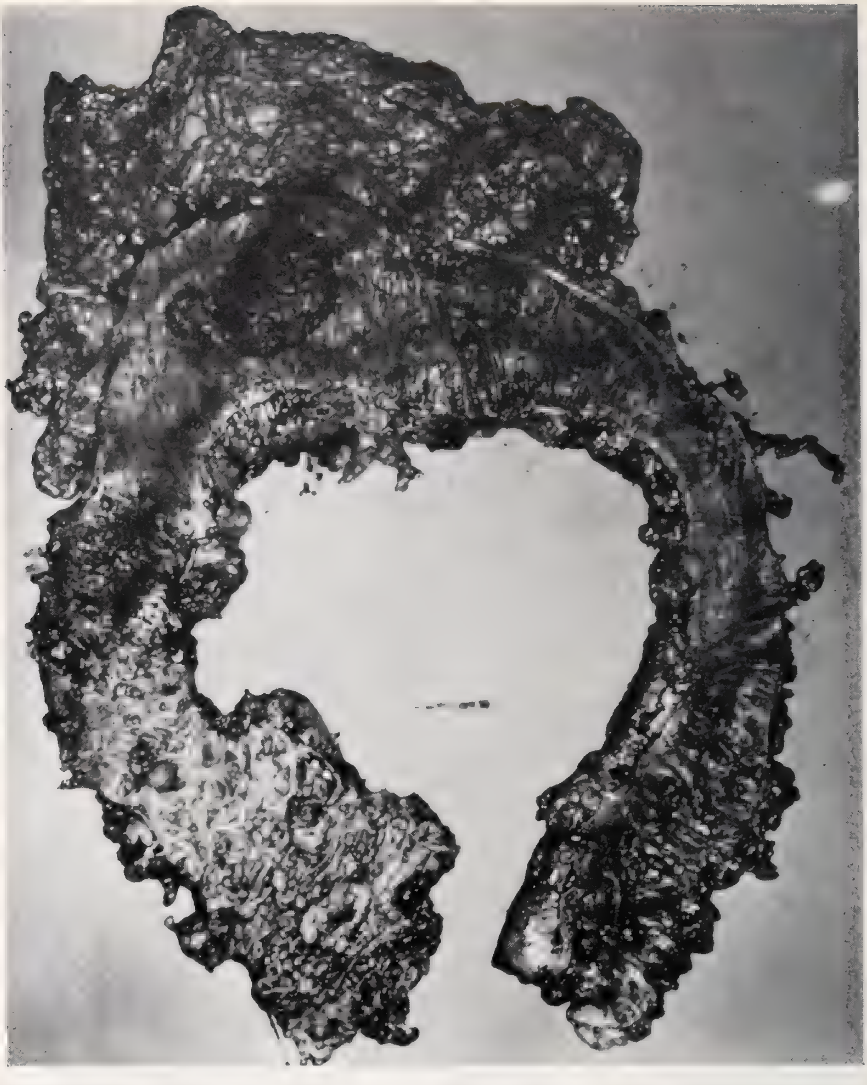

FIG. 5. Specimen of entire colon showing diffuse polyposis. The adenomas, sessile and polypoid, show a wide range in size.

erupted teeth which should have appeared on the surface several years prior to the examination (Fig. 11). Sigmoidoscopy and barium enema examination have disclosed no polyps to date.

This patient is included as a case of true Gardner's syndrome according to the criteria of Thomas et al who believe that cases of Gardner's syndrome fall into one of two categories; (a) all three manifestations present with or without a positive family history or (b) one or more of the triad of soft tissue tumors, bony tumors, or colonic polyposis present in a patient in whose family there are members with the complete triad (2).

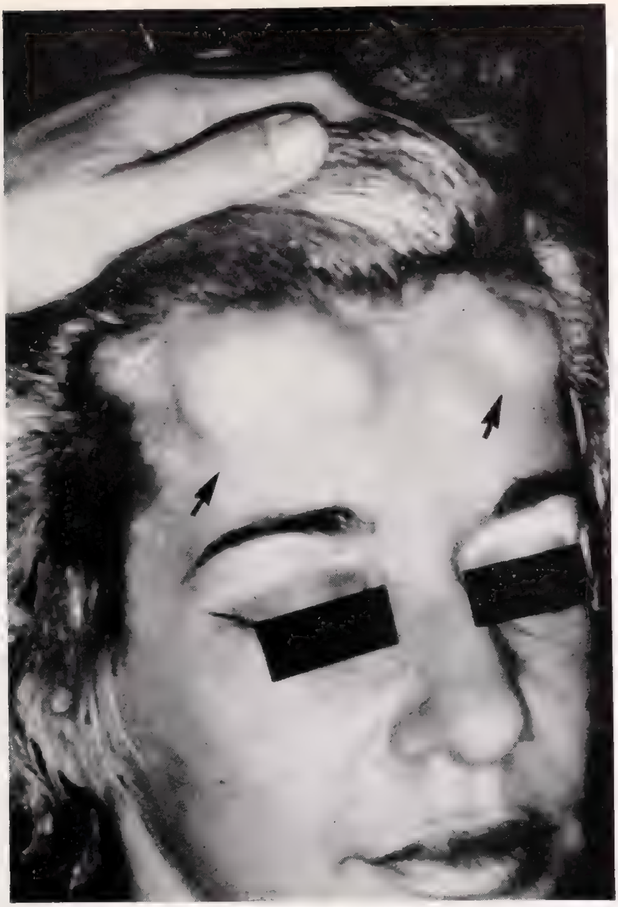

FIG. 6. Osteomas of skull. Case 2.

Discussion

Symptoms: There are very few symptoms in the early stages of Gardner's syndrome. The passage of several mucous stools a day is hardly noticed and is accepted as a normal situation by many patients. Rectal bleeding is usually mild. Patients feel noticeably fatigued only after the hemoglobin falls below 7 or 8 grams.

Signs: Other tumors besides osteomas, epidermoid cysts, and fibromas (desmoids) have been reported but are much less common. These include lipomas, leiomyomas, neurofibromas, mesenteric fibrous masses, and retroperitoneal fibrous or mixed tumors (3). The visible and palpable extraintestinal tumor manifestations are generally established at puberty prior to the colonic polyposis or the onset of significant gastrointestinal symptoms. The osteoma present at birth in Case 3 is possibly unique; we are not aware of any previously documented case reported in the literature.

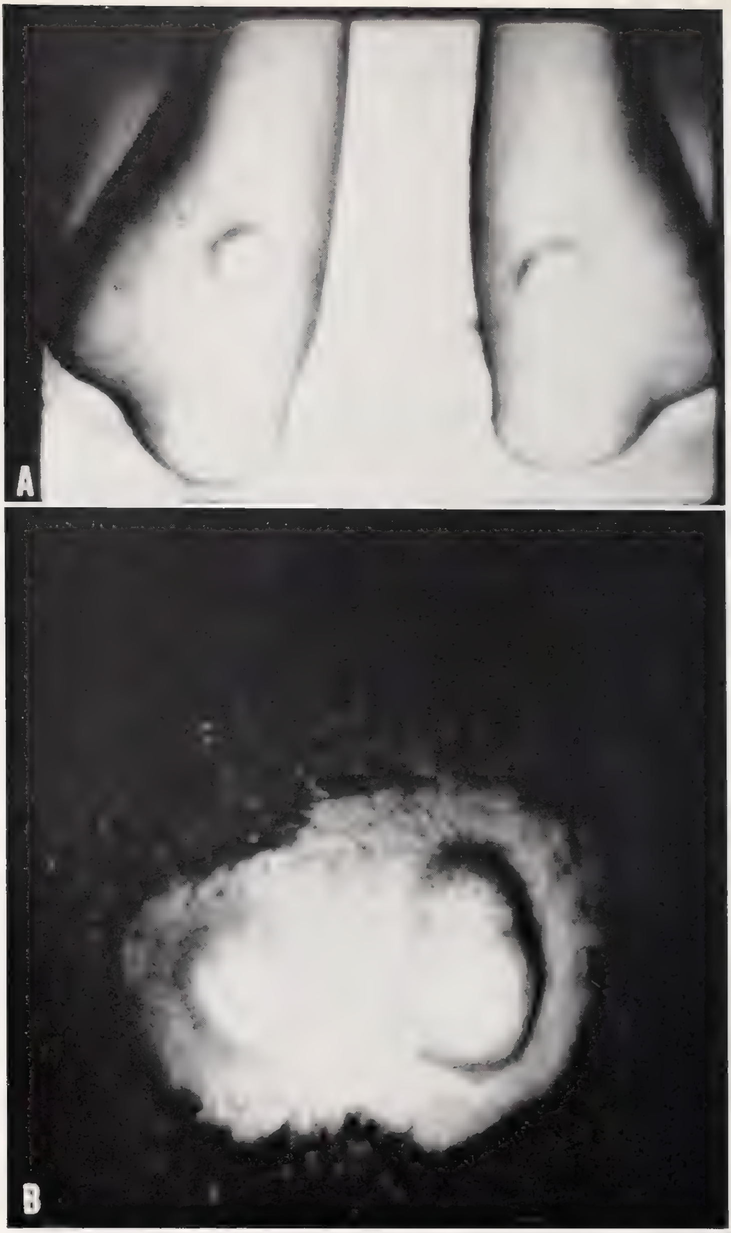

Fig. 7. a) Symmetrical cysts of forearms, case 2. b) Sebaceous cysts of the scalp, case 3.

The dental abnormalities include supernumerary teeth, delayed or permanently unerupted teeth, dentigerous cysts, and medullary bone thickening of the mandible and maxilla with effacement of the trabecular pattern.

X-ray Examination: Osteomas are most commonly seen in the skull, man-

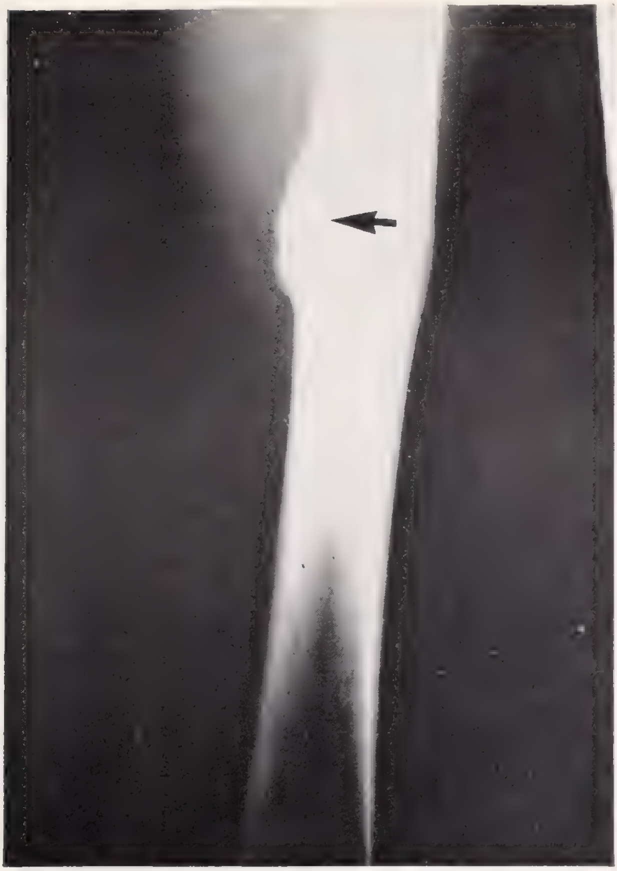

FIG. 8. Osteoma of femur. Case 2.

dible, sinuses, and long bones. Nevertheless, a complete skeletal survey should be performed to disclose osteomas which may be found in the digits, ribs, and other smaller bones.

The barium enema is often difficult to interpret. In Cases 1 and 2, there was difficulty in distinguishing groups of polyps from retained fecal material despite the restriction of diet to clear fluids and the use of cathartics over a period of 2 days before the barium enema was performed. The air contrast roentgenogram is the most important study to demonstrate the smaller polyps.

Pathology: The size and number of polyps found depend, to a large extent, on the age of the patient. Older individuals generally have more and larger polyps. The polyps may be diffuse throughout the colon or heavily concentrated in one segment of the colon with only a few scattered elsewhere in the large intestine.

Surgical Management: Colonic surgery should be performed when the diagnosis of multiple polyposis is apparent. A complete removal of the entire colon and rectum with permanent ileostomy is performed when the rectal pathology

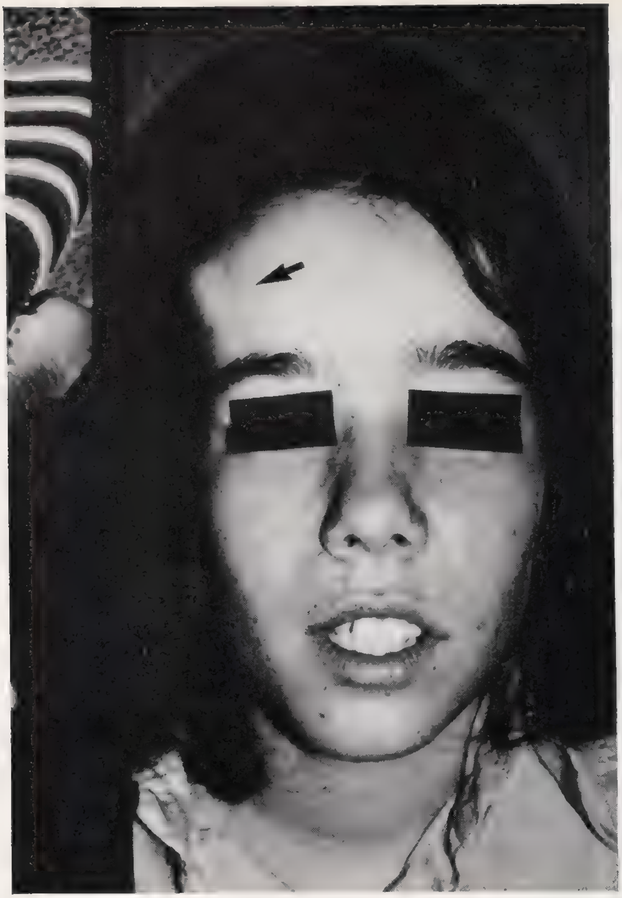

FIG. 9. Osteoma of skull. Case 3.

is too diffuse, the patient is uncooperative and unlikely to return for observation, and when rectal cancer is already present.

When a total colectomy and ileorectal anastomosis is performed, not more than 8 inches of rectum should be left behind. An end-to-end ileorectal anastomosis is preferred because the potential complications of a blind pouch are avoided and any recurrent rectal polyps are easily visualized and destroyed. Postoperatively, sigmoidoscopic examination is performed every 3 months. If no recurrent rectal polyps are seen after 2 years, the examination may be done every 6 months.

Prognosis: Every person with untreated diffuse familial polyposis of the colon will usually be dead or have advanced malignant disease of the colon or rectum before he reaches the age of 50.

Extirpation of the entire colon and rectum before cancer develops eliminates the possibility of cancer of the large intestine and precludes the necessity for

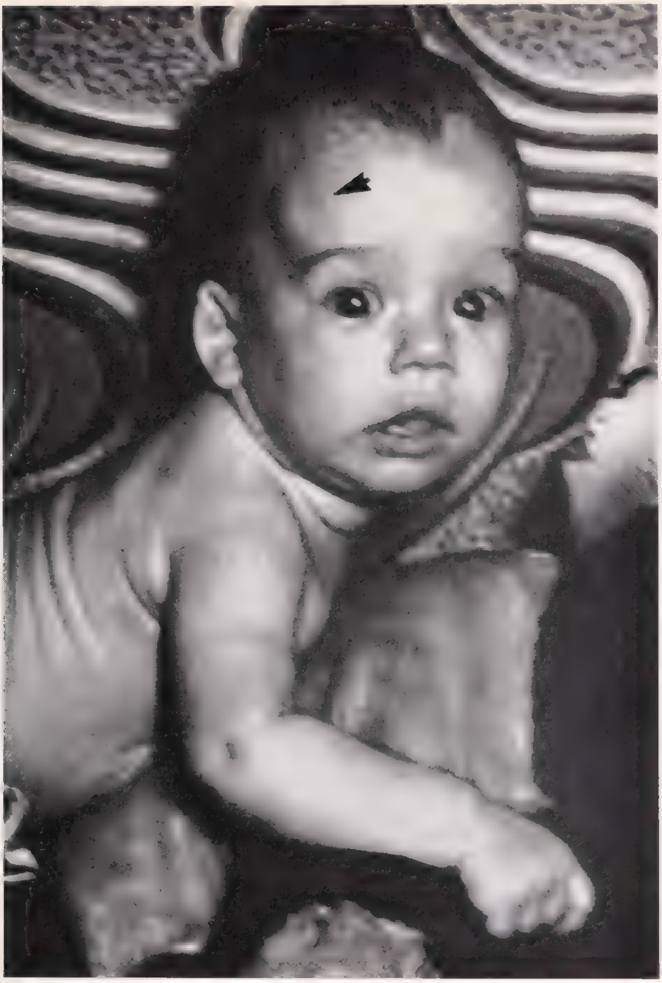

FIG. 10. Osteoma of skull at age 6 months. Case 3.

rectal fulguration and frequent long-term observation of the rectum for recurrent disease. However, it leaves the patient with the burden of lifetime care of an ileostomy with its potential complications.

Even if followed carefully, many will develop cancer of the remaining rectum when the rectum is left behind. At times there is a spontaneous disappearance of rectal polyps after colectomy and ileorectal anastomosis (4).

Stricture of the rectum, resulting from scarring secondary to repeated fulguration may require further surgery.

Conclusion: Earlier diagnosis of familial polyposis of the colon is made possible by noting the extraintestinal manifestations which are present in Gardner's syndrome.

The presence of osteomas, multiple epidermoid cysts, and fibromatous (des-

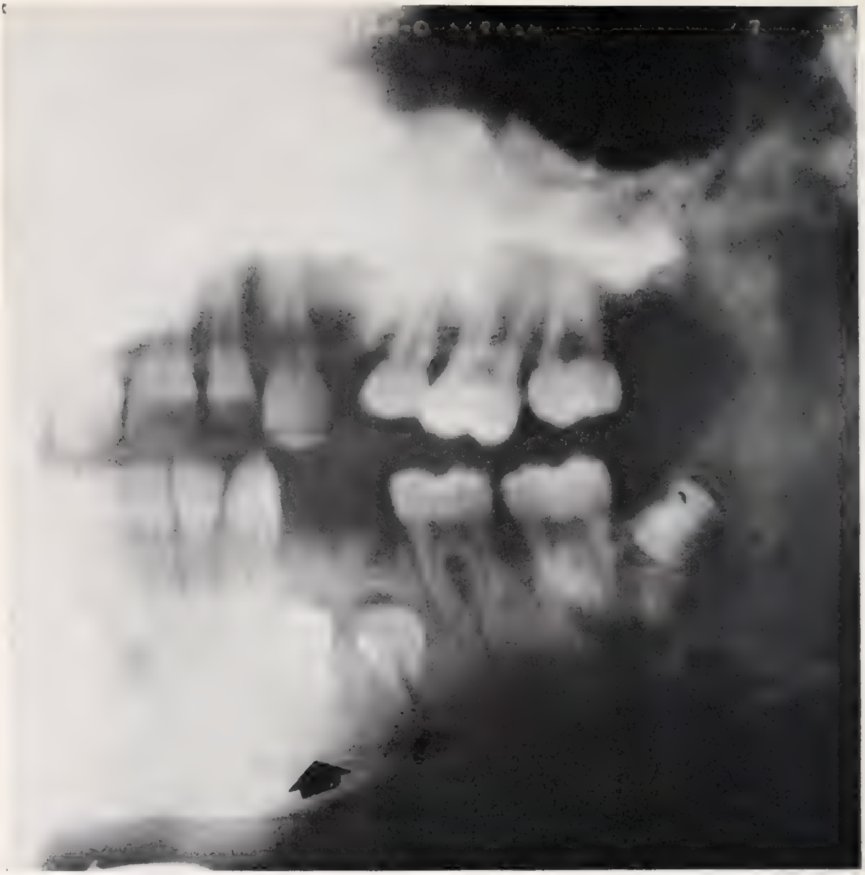

FIG. 11. Unerupted teeth and osteomatosis of the mandible with effacement of trabecular pattern.

moid) masses are indications for sigmoidoscopy and barium enema studies despite the absence of gastrointestinal symptoms.

A positive diagnosis of Gardner's syndrome in one patient mandates an investigation of all the members of a family group for evidence of this disease.

Credits

Dental consultation: Richard Moskow D.D.S. and Roger G. Gerry D.D.S. Roentgenography: Arthur Lautkin M.D. and Elliot Greenberg M.D. Clinical research supported by the Stella and Charles Guttman Foundation.

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OPHTHALMOLOGICAL NOTES

THEODORE W. LIEBERMAN, M.D., EDITOR

Lens Findings in Patients with Myasthenia Gravis on Long-Term Treatment with Oral Anticholinesterases

BY THEODORE W. LIEBERMAN*, M.D., IRVING H. LEOPOLD*, M.D.,
KERMIT E. OSSERMAN†, M.D. AND LYON HYAMS, M.D.‡

An association between the development of lenticular opacities and the prolonged ocular instillation of long-acting anticholinesterases has been reported by several authors (1–11). The typical lens changes described are anterior subcapsular vacuoles usually arranged in clusters, streaks, or irregular groupings, and anterior subcapsular mossy opacities. Posterior subcapsular vacuoles and opacities, and nuclear sclerosis have been reported. Although anterior and posterior subcapsular changes often occur in the lenses of untreated individuals over the age of 40 years (2, 6, 11, 12), an increased incidence of these findings has been found in adult patients being treated for glaucoma with long-acting anticholinesterases. A few isolated case reports describe similar lens changes in children treated with anticholinesterases for accommodative esotropia (8, 13, 14), but this finding is uncommon (15).

Echothiophate iodide (Phospholine Iodide®) has been most frequently investigated in regard to lens changes. Demacarium bromide (Humorsol,® Tosmilen®) (6, 7), paraoxon (Mintacol®) (2) and diisopropyl fluorophosphate (DFP, Floropryl®) (6, 13) have also been implicated in producing lens opacities.

Myasthenia gravis is a disease characterized by weakness and easy fatigability which affects the general skeletal, extrinsic eye, facial, pharyngeal, laryngeal, and respiratory muscles. Since Mary Walker (16) in 1934 first described improvement in the muscular strength of patients with myasthenia gravis on administering physostigmine, the oral administration of anticholinesterases has been the mainstay of myasthenia gravis therapy (17, 18). The present investigation was conducted to determine if the long-term oral administration of anticholinesterases produced lens changes similar to those ascribed to the local ocular instillation of this class of drugs.

Materials and Methods

Fifty-five patients (40 women and 15 men) with myasthenia gravis were given eye examinations. Four or five patients were randomly selected for study at each session of the Myasthenia Gravis Clinic of The Mount Sinai Hospital.

From the Departments of Ophthalmology* and Medicine† and the Myasthenia Gravis Clinic and Research Laboratory,† Mount Sinai School of Medicine of The City University of New York, N.Y. 10029; and from the Division of Biostatistics, Department of Community Medicine, Rutgers Medical School, Rutgers, The State University.‡

This investigation was supported by PHS Research Grant No. EY 00340 from the National Eye Institute, Bethesda Md., and by the Tillie Lewis Foundation.

One eye of one patient was excluded from the study because of a mature cataract and evidence of an inactive uveitis.

The age distribution of these study patients is shown in Table I and the duration of their myasthenia in Table II. Sixteen patients had thymectomies (10 women and 6 men).

Large amounts of anticholinesterase therapy were used in this group of patients. The type, duration, and total dosage of oral anticholinesterase therapy administered is listed in Table III. The term pyridostigmine (Mestinon®) equivalent has been used to estimate total anticholinesterase therapy. Sixty mg of pyridostigmine (Mestinon®) equivalent has been considered similar to a

TABLE I

Age Distribution of 55 Study Patients with Myasthenia Gravis

Age (Years)	Number of Patients Examined
0–20	3
21–40	25
41–60	15
61–80	12

TABLE II

Duration of Disease in 55 Study Patients with Myasthenia Gravis

Duration of Disease	Number of Patients
<1 year	5
1 year to < 5 years	15
5 years to <10 years	13
10 years to <20 years	11
20 years to 30 years	11

TABLE III

Anticholinesterase Therapy Used in 55 Study Patients with Myasthenia Gravis

Drug	Pyridostigmine	Pyridostigmine Timespan	Neostigmine	Ambenonium Chloride	Echothiophate Iodide	Total Dose Pyridostigmine Equivalent*
No. pts.	48	19	18	8	2	55
Average months of therapy	53.1	45.7	85	18.6	77.5	84.5
Range (months)	1–168	3–132	1–267	1–72	77–78	0**–324
Average Total Dose (grams)	863	1235	357	24.9	5.6	1411
Range (grams)	82–7004	16–10,530	6–1405	1–65	2.9–8.2	0**–8732

* 60 mg pyridostigmine equivalent = 60 mg of pyridostigmine; = 180 mg of pyridostigmine timespan; = 6 mg of ambenonium chloride = 15 mg of neostigmine; = 1 mg of echothiophate iodide.

** One patient received no therapy.

dosage of 60 mg of pyridostigmine (Mestinon®), 180 mg of pyridostigmine (Mestinon®) timespan, 6 mg of ambenonium chloride (Mytelase®), 15 mg of neostigmine (Prostigmin®), and 1 mg of echothiophate iodide (Phospholine Iodide®). The distribution of the daily pyridostigmine (Mestinon®) equivalent dosages which patients were receiving at the time of the study is shown in Table IV.

The visual acuity was taken with glasses if these were available. Best corrected visual acuity was estimated with a multiple pinhole disk. The examination also included an evaluation of eye movements, levator palpebrae and orbicularis oculi function, and of pupillary size and reactions. The intraocular pressure was measured with a Schiøtz tonometer with the patient in a supine position. Slit lamp examination was performed before and after the pupils were dilated with 1% tropicamide (Mydriacyl®) and 2½% phenylephrine hydrochloride (Neo-Synephrine®).

The fundi were examined after dilation. The lens of each eye was examined carefully with specific use of retroillumination in order to avoid missing small vacuoles. Lenticular changes were categorized and recorded on printed coronal and sagittal sketches of the lens.

Cortical dot opacities were frequently observed. Each patient was graded into one of four categories (0, 1, 2, 3) depending on the number of dot opacities present in each lens. Table V presents the criteria of classification and the distribution of patients within these groupings. The patients could be arranged in this way because the grade of dots found in the lenses of the two eyes of individual patients was nearly always the same. Only eight of 55 patients studied showed a discrepancy between eyes and these were usually of a one-level difference.

We related these groupings to five other variables obtained from each subject. These were 1) present age, 2) sex, 3) duration of disease, 4) thymectomy or not, and 5) four parameters of dosage: average, monthly, total, and recent daily dosages, and duration of therapy. Such a simultaneous evaluation is possible within the methodological framework of a discriminant function analysis (19, 20).

This approach evaluates whether it is possible to show a statistically signifi-

TABLE IV

Daily Drug Dosage in Terms of Pyridostigmine (Mestinon®) Equivalent at Time of Study

Pyridostigmine Equivalent Dosage (mg/day)	No. of Patients
0	6
1–100	3
101–200	9
201–300	15
301–400	2
401–600	8
601–800	6
801–1400	6

TABLE V

Classification and Frequency of Cortical Lens Opacities in 55 Study Patients with Myasthenia Gravis

Classification	No. of dots/lens	No. of patients	% of patients
0	≦10	18	32.7
1	11–50	22	40.0
2	51–100	11	20.0
3	>100	4	7.3
Total		55	100.0

TABLE VI

Type and Frequency of Lens Opacities and Their Effect on Visual Acuity in 55 Myasthenia Gravis Patients on Oral Anticholinesterase

Type	No. of Eyes	No. of Patients	Average Age	Average Visual Acuity*
Anterior subcapsular vacuoles	3	2	54	.82
Cortical spokes clefts	9	6	65	.78
Nuclear sclerosis	15	8	61	.63
Unclassified (lamellar cortical discs)	2	1	21	.58
Posterior polar opacity	1	1	62	.50
Cerulean opacities	6	3	35	.82
Y suture opacities	7	4	29	.60
Embryonic nuclear opacities	4	3	44	1.0
Cortical dot or punctate opacities				
Grade 0**	34	19	35	.76
Grade 1	47	26	43	.80
Grade 2	20	12	52	.74
Grade 3	8	6	42	.79

* Average visual acuity is mean of decimal equivalent of visual acuity E.G. 20/15 = 1.33; 20/20 = 1; 20/25 = .80 20/40 = .50 20/100 = .20.

** Grade 0, ≦ 10 dots/lens; Grade 1, 11–50 dots/lens; Grade 2, 51–100 dots/lens; Grade 3 >100 dots/lens.

cant difference between the patients classified as grade 0 versus those patients having either grade 2 and 3* cortical dots using some linear combination of the variables measured. In addition, if a significant difference can be found between grades 0 and the combined grades 2 and 3 lens dots, the discriminant analysis pinpoints those variables necessary to obtain such a separation and indicates which ones are most important.

Results

Table VI lists the various types of lens opacities observed during this study. Only three eyes (two patients) showed one or two discrete isolated subcapsular vacuoles. Clusters of vacuoles and subcapsular mossy opacities were not seen. No posterior subcapsular opacities were noted. Peripheral cortical spokes and nuclear sclerosis were only seen in older patients, and in all study cases were in their early stages of development.

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* Grade 1 cortical lens dots were not used in this analysis to permit a greater separation of data.

Cortical dot opactities were seen in many patients, but did not appear to interfere with visual acuity (Table VI). The visual acuities taken in these patients can only be considered approximations. Some patients had constantly patched one eye or left an eye covered by a ptotic lid to avoid diplopia. Other patients had severe ocular motility problems and the head had to be rotated to bring the visual axis into alignment with the chart. Still other patients had insufficient muscular strength to hold the pin-hole disk steady. These problems led to poor performance in obtaining accurate visual acuities.

Of the eight variables used in the discriminant analysis only four were found to correlate with the severity of lens opacities. In order of descending importance these were: age, average monthly dosage of drug, thymectomy or not, and sex. The relationships between these parameters and the severity of lens dot opacities are given in Table VII. The number of dots increased with older age, greater average monthly dosage of drug, femaleness, and the presence of the thymus.

The mean intraocular pressure was 15.7 mm Hg (standard deviation = 3.75, N = 87). Many patients showed orbicularis oculi and levator palpebrae weakness, as well as limitation of eye movements. No unusual fundus abnormalities were noted.

Discussion

The incidence of anterior and posterior subcapsular vacuoles and opacities is extremely low (3%) in the group of patients studied despite large daily and total dosage of anticholinesterases. From 30% to 50% of glaucoma patients on topically instilled anticholinesterases administered over several years have been reported to develop lens changes. This difference may in part be accounted for by much lower concentrations of anticholinesterases reaching the ocular tissue when the drugs are administered by the oral route rather than by local administration. The fact that only two patients in the study had miotic pupils suggests low ocular concentrations of the anticholinesterases were present.

The small number of patients showing lens changes having any resemblance to those reported due to local anticholinesterase administration is against the suggested concept that the lens opacities may be related to a reduction of serum pseudocholinesterases or red blood cell cholinesterase (4). Patients with myasthenia gravis on oral anticholinesterases have been shown to have depressed serum and red blood cell cholinesterase levels (21).

In agreement with our findings, Cinotti and Patti (12) found that cortical dot opacities and spokes increased with age and were more prevalent in normal females (23.0%) than in normal males (9.7%) over the age of 40 years. The preponderance of females in the study is in keeping with the higher incidence of myasthenia gravis in females (22). The meaning of the increased incidence of cortical dot opacities to high average monthly doses of medication and to the presence of the thymus is not clear and may be more directly related to the overall and long-term severity of the disease rather than to the specific parameters analyzed.

TABLE VII

Relationship Between Severity of Cortical Dot Opacities in 55 Myasthenic Patients and Significantly Related Variables (Age, Average Monthly Dose, Sex, and Thymus Ablation)

Age (years)	Eyes by Grade Cortical Dots				
	Grade 0		Grades 2 & 3		Totals
	Percent	No.	Percent	No.	No. Eyes
A. Age					
0–20	100	(6)	0	(0)	6
21–40	64	(16)	36	(9)	25
41–60	50	(8)	50	(8)	16
61–80	26	(4)	74	(11)	15
Total Eyes		34		28	62
B. Average Monthly Dose					
Average Monthly Dosage (grams)*					
0–11.5	79	(23)	21	(6)	29
11.5+	33	(11)	67	(22)	33
Total Eyes		34		28	62
C. Sex					
Sex					
Female	49	(19)	51	(20)	39
Male	65	(15)	35	(8)	23
Total Eyes		34		28	62
D. Thymic Ablation					
Thymic Status					
Present	26	(20)	74	(57)	77
Ablated	44	(14)	56	(18)	32
Total Eyes		34		75	109

* pyridostigmine equivalent

Summary

In a study of 55 myasthenia gravis patients on long-term oral anticholinesterase therapy only 2 patients were found to have lens changes which in any way resembled those described after the long-term use of local anticholinesterase for glaucoma. Cortical punctate opacities in the lenses were common. They did not interfere with vision and were most highly correlated with the age of the patient. They may also be related to factors associated with myasthenia gravis and/or its treatment.

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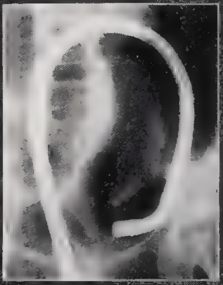

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In Memoriam

MAURICE EUGENE WOLF, M.D.
1895–1970

Dr. Maurice E. Wolf, an Assistant Attending Physician at The Mount Sinai Hospital, and for many years until 1962, Chief of its Arthritis Clinic, died on November 30, 1970.

Dr. Wolf was born August 11, 1895 in Colmar, France. After completing his medical studies at the University of Strasbourg, he began a distinguished medical and academic career at this ancient and famous medical school. He was successively Lecturer in Anatomy, Chief of the Medical Clinic in the Professorial Unit of Prof. Ambard, and was appointed Professor of Medicine in 1929.

During his academic activities he engaged in intense research. In collaboration with Prof. Pierre Mason he worked on hematopoietic tumors; he did a study of the physiopathology of the liver with Prof. Noel Fiessinger. In 1923 his "Contribution to the Study of Cancer" was published in *The Treatise on Cancer* in collaboration with Prof. Gustave Roussy, the famous French pathologist. During that and the previous year, he held the post of the First Assistant in the Medical Professorial Unit at the Faculty of Medicine of the University of Paris.

When the war broke out in 1939, Dr. Wolf joined the Medical Corps of the French Army, in which he served as a Medical Specialist. After the collapse of France, he came to this country with his family in 1942 and soon after he began his association with The Mount Sinai Hospital and its Arthritis Clinic.

Dr. Wolf had always had a major interest in rheumatology. After his arrival in this country he devoted himself principally to the study and treatment of rheumatic diseases, although interested in all aspects of internal medicine. Besides his very busy private practice and his service in Mount Sinai, he also served as Chief of the Arthritis Clinic and Visiting Physician at the City Hospital Center at Elmhurst for many productive years.

An excellent physician, his main qualities were, however, of a broader, more humanistic nature. His warmth and personal approach made him beloved by his innumerable patients. He was not only their doctor, he was a friend. If he could not cure his patients, he always gave them comfort and hope.

He was a man of great culture and manifold interests. He traveled all over the world. He was interested in art, modern and ancient; and he was the proud owner of a small, but exquisite collection of paintings and pre-Columbian sculptures. He was a man of great courtesy and charm and of great moral courage. For many months he knew that his illness was fatal, but he continued to work and to treat his patients almost until the last days of his life.

Dr. Wolf had a happy and enjoyable life in his adopted country; he was an

MAURICE EUGENE WOLF, M.D.
1895–1970

American, but he never forgot France. He visited the country of his birth frequently, and, in recognition of his services to the Franco-American cause, the French Government awarded him the Cross of Commander of the Legion of Honor.

Medicine is the poorer for his passing, as are all of those who knew him.

Samuel Katz, M.D.
for the
Editorial Board

Some Remarks about Hyperbaric Oxygen Treatment and about Artificial Organs in the 1970's

W. J. KOLFF, M.D., PH.D.*

Around 1932, according to a newspaper clipping illuminated with photographs, a Canton manufacturer, Mr. Timken, built an entire hospital for the treatment of patients with oxygen under high pressure. The caption over the article says that the cost of the hyperbaric hospital was one million dollars and that it was to aid sufferers of diabetes. Under the caption it said that this was a secret treatment discovered by a Kansas City doctor.

Secrecy in experimental medicine rarely pays off. This magnificent hospital indeed existed. It had a long cylindrical part and a large spherical part. The sphere contained five stories and in the upper story was a billiard room. The entire structure, hospital rooms, corridors, pool room, was all under high pressure; I have personally spoken with somebody who was in it, and who was given oxygen with an oxygen mask until he developed convulsions. When steel was in short demand during World War II the hospital was scrapped. I came to Cleveland from the Netherlands in 1950, and when I learned that the entire structure had been destroyed I could have cried. Boerema in the Netherlands had worked with the hyperbaric oxygen with such success that it forced the American medical community to pay attention. But the magnificent facility came to naught for the simple reasons that there was insufficient scientific background and that it was conducted in secrecy.

Immediately one sees the contrast with the situation which has been created here by appointing Dr. Converse Peirce to become the first Henry Kaufmann Professor of Hyperbaric Surgery. There is nothing secret about Dr. Converse Peirce. There is nothing unscientific about Dr. Converse Peirce. He is deeply interested in the physiological phenomena in acid-base metabolism and in every scientific aspect which can be correlated with the use of oxygen under high pressure.

High pressure oxygen treatment can be combined with a multitude of advanced medical techniques. It can be life-saving in otherwise refractory infections with anaerobic bacteria. It can be applied in combination with cooling or hypothermia so that the circulation can be arrested, and I hope to use this to implant artificial hearts, about which I will tell you later. It can be applied to the preservation of organs—for example, kidneys that are to be transplanted. It is advantageous to remove cadaver kidneys in a hyperbaric oxygen chamber so that they can be used for transplantation.

In 1947, while I still lived in the Netherlands, I sent an artificial kidney to

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Excerpts from presentation at investiture of Dr. E. Converse Peirce II as Henry Kaufmann Professor of Hyperbaric Surgery, the Mount Sinai School of Medicine of The City University of New York, October 23, 1970.

* Head, Division of Artificial Organs, College of Medicine, University of Utah, Salt Lake City, Utah.

The Mount Sinai Hospital. It became the first artificial kidney to be clinically used in the United States (1). Dr. Fishman and Dr. Kroop from this hospital published a paper to prove that the artificial kidney could be applied in people other than the Dutch (2). Presently 3,000 people are being treated with artificial kidneys in the United Sates. This is only a fraction of the number of people who should be treated. It is a disgrace to this country that selection committees still determine whether a patient shall live or shall die on the basis of social criteria.

The artificial kidney runs blood outside the body through a dialysis machine. You must, therefore, have access to the blood vessels. The arteriovenous shunt cannulas introduced by Scribner made possible the maintenance dialysis of patients in chronic renal failure. More recently the creation of an arteriovenous fistula, that is, a connection between an artery and a vein, introduced by Dr. Cimino, made it possible to puncture the distended veins of the patient for each treatment, and it is now possible to eliminate the permanently in-dwelling cannulas in the arm. It is expected that during the seventies we will see more and more use of the these AV fistulas and with them a new danger is introduced. That is the danger of air embolism. Since a pump is required to suck the blood from the vein, there is a possibility that air will be aspirated if the blood supply is insufficient. A bubble detector in the venous return line recently developed in our laboratory, we hope, will save patients' lives. (See Figure 1.)

The seventies will undoubtedly see the introduction of mechanical assist devices to the heart and circulation. Many are presently being developed and tested in the laboratory. Whereas great strides have been made in the treatment of victims of coronary heart disease by means of drugs and electrical treatment, the progress of mechanical assist devices to help these people is being pursued very reluctantly. Yet for the patients in cardiogenic shock (the actual pump failure of the heart's inability to carry the circulation) the prognosis is almost uniformly death. The number of patients who die each year from coronary heart attacks is approximately 600,000. How many of these could be saved by mechanical assist devices depends largely on how quickly they can be applied.

The incubation time (between invention and clinical application) for these methods is distressingly long. Seven years passed before balloon pumping in the aorta, which was introduced by Moulopoulos and Topaz in our laboratory in 1961, was seriously applied clinically by Dr. Kantrowitz in Brooklyn. I hope that a method recently developed by Dr. Hans Zwart will not have to go through such a long incubation time because it might save thousands of lives.

Dr. Hans Zwart, while still in the Netherlands, introduced a stainless steel cannula into the left ventricle and so doing, removed the blood from the failing left ventricle and pumped it back into the femoral artery. This is the only method by which the failing ventricle can be decompressed and the circulation can be maintained even when the heart is in ventricular fibrillation. When this young Dutchman joined me about two years ago, the first thing I had him do was make a cannula which could apply this method in human beings. (See Figure 2.) So far two patients have been treated, but numerous sheep (of the

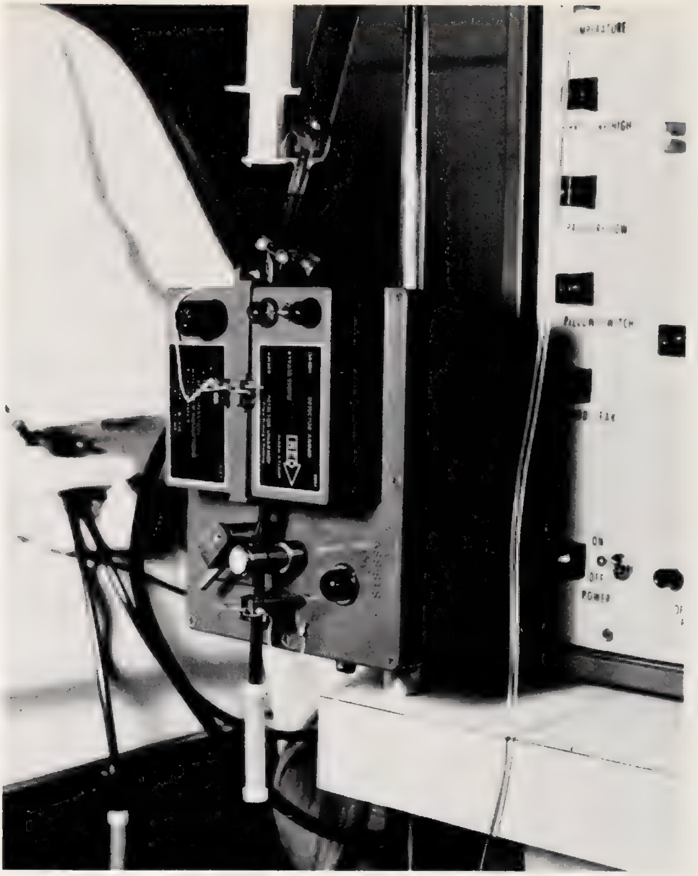

FIG. 1. A bubble detector clamp which will detect air bubbles in the venous return line from the artificial kidney toward the patient will sound an alarm, blink a light, clamp the line, and stop the blood pump. The excuse for showing this picture in a scientific journal is that it is a life-saving device. The occurrence of air emboli has greatly increased since the A-V fistula has gained in popularity.

same body weight as potential victims of coronary heart disease) have been subjected to transarterial bypass with, I believe, outstanding success. It is my personal opinion, therefore, that this method is now ready for large clinical trials in otherwise desperate cases dying from coronary heart attacks. I am very gratified that Dr. Leslie A. Kuhn and coworkers from the Mount Sinai School of Medicine are reporting their excellent results at the meeting of the American Heart Association this month.

After the successful transplantation of a human heart in South Africa, many surgical laboratories and heart surgeons began to transplant hearts. With the exception of the experience of Dr. Shumway in Palo Alto, who was the originator of the technique, the overall clinical success has not been encouraging, and a wave of pessimism has swept over the cardiovascular surgeons and their laboratories in this country and all over the world. Why don't they gird themselves

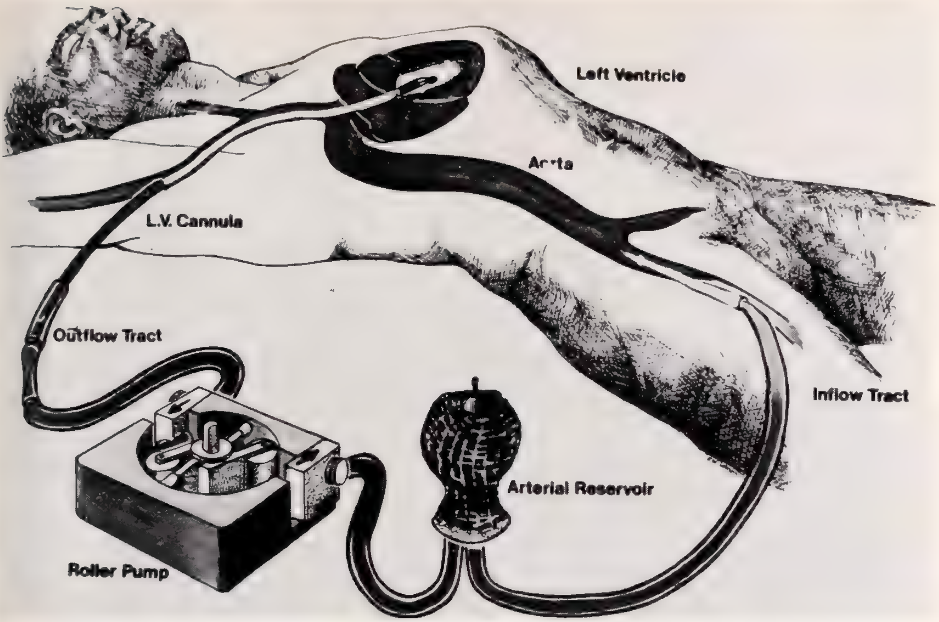

Fig. 2. Transarterial Closed-Chest Left Ventricular Bypass. Using a flexible cannula, the blood is sucked out of the left ventricle and pumped back in a femoral artery. With this method, it is possible to sustain the circulation even if the ventricles are fibrillating. Perfusion of the lungs by venous backpressure is sufficient at least for several hours. (*Journal of Association for Advancement of Medical Instrumentation*)

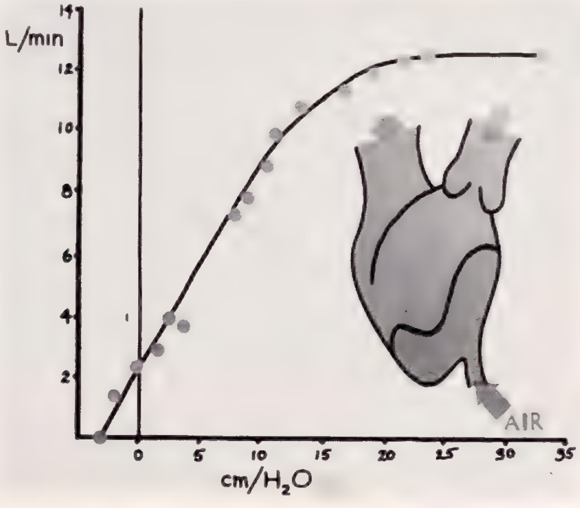

Fig. 3. One type of artificial heart, driven by compressed air which enters the chest wall through a tube. A cross section of the left ventricle is shown. This is the Kolff-Kralios-Kessler type of artificial heart. The curve indicates that the cardiac output increases with the atrial pressure, which is expressed in cm of water. This is Starling's Law of the artificial heart. In our artificial heart, this can be accomplished without electronics inside the chest. (*Trans. ASAIO, 1970, Vol XVI*)

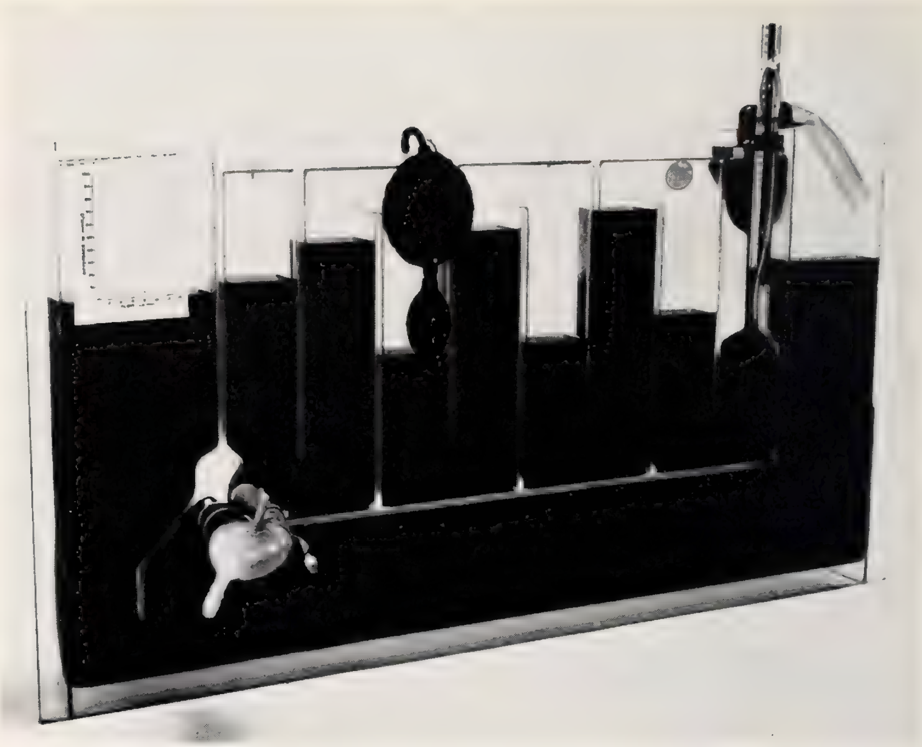

Fig. 4. Photograph of a mock circulation in which an artificial heart can be tested. *(Trans. ASAIO, 1970, Vol XVI)*

and make a contribution to the application of the artificial heart? (See Figures 3 and 4.) The equipment is now available, at very nominal cost. (See Figure 5.) We recently had a calf that liver for 92 hours after removal of its own heart and implantation of an artificial heart. (See Figure 6.)

The idea of an artificial eye which can really see is, of course, the hope of a good many blind people and their families. It is not available yet, but I would like to show you the first modest steps which are being made in this direction. They follow the original work by Brindley in England. One member of our group in Salt Lake City, Mr. William Dobelle, travels from Salt Lake City to places in the country where there are patients needing to have the skull opened for operations in the occipital area of the brain. With the cooperation of the neurosurgeon and the permission and cooperation of the patient who is under local anesthesia, he can now stimulate discrete areas of the brain and the patient will indicate that he sees a light and where. So far, we know that if he stimulates one point the patient will consistently see a light spot at one point in his visual field. It can thus be hoped that a computer can translate the half tone image of a television camera into a number of discrete points so that the patient might get a useful visual sensation. Contrary to what many people believe to be the most important, blind people invariably state that it is not

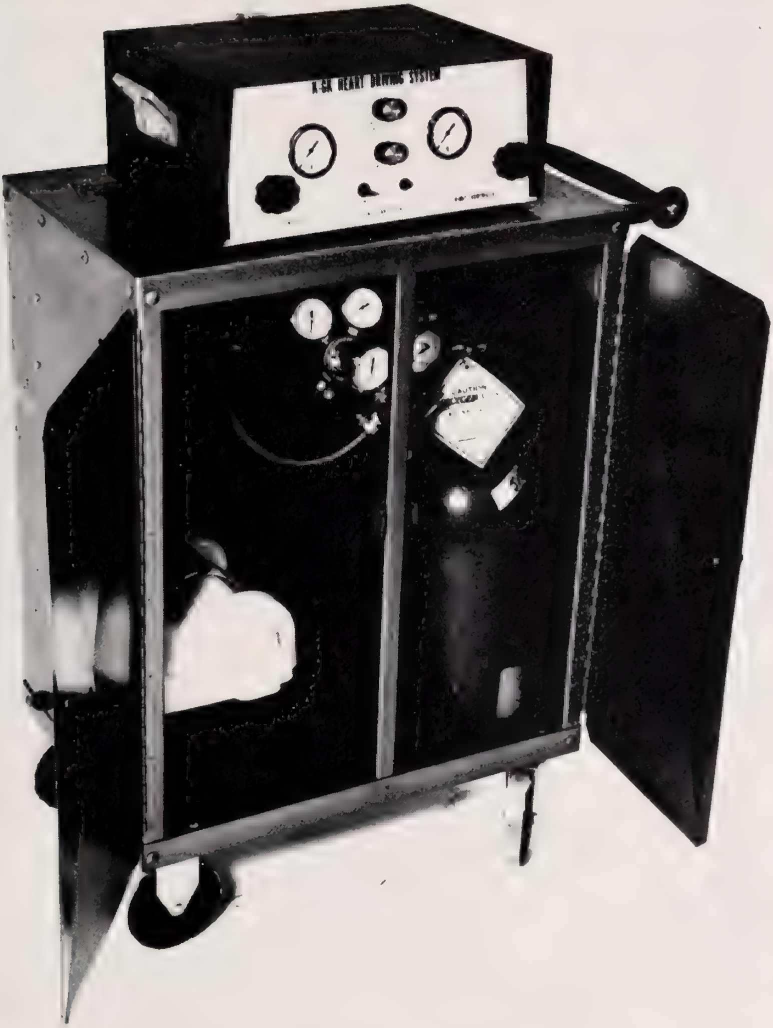

Fig. 5. K-G-K Heart Driving System. The heart rate and duration of systole can be set. The cart provides the compressed gas which can drive the artificial heart for about four hours, thus providing a certain degree of portability. A battery will automatically take over any time the line current is interrupted. (*Trans. ASAIO, 1970, Vol XVI*)

reading which they need as much as a device that will enable them to move around. Indeed, one may conceive a television camera small enough to fit in the socket of an eye.

Whether you like it or not, technology has now advanced to the point where it is possible to perfuse the head of an animal, and therefore the head of a man, after it has been separated from its body. I am quite sure that Dr. Converse Peirce, who has built artificial kidneys, oxygenators, and blood pumps, could perform this act without any trouble. I did not say that it is desirable. It may

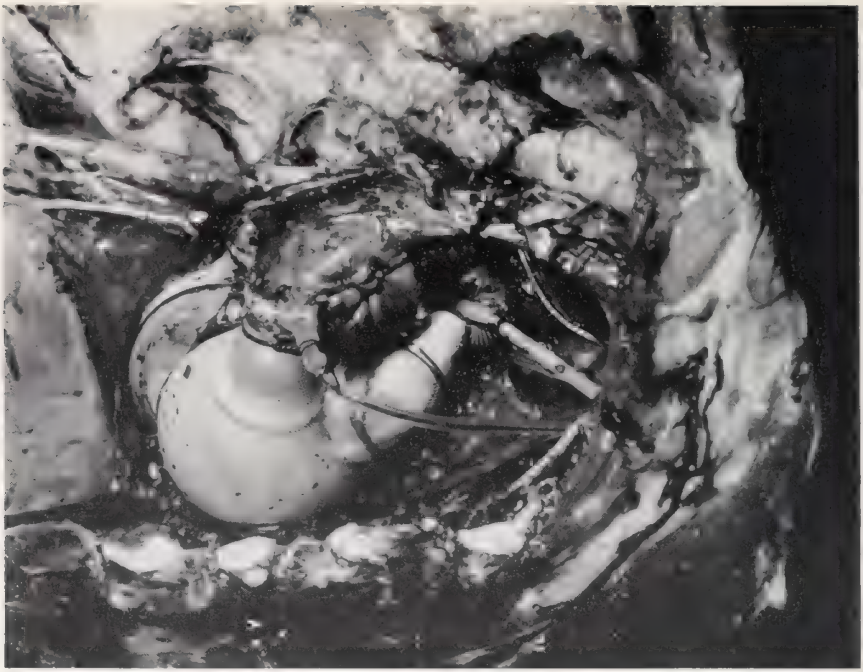

FIG. 6. The Kwan-Gett type of artificial heart inside the chest of a calf at the end of an experiment. While the carcass of the animal is suspended in a natural standing position, the front legs and lateral chest wall have been removed so that the connection of the artificial heart with the vena cava and the other blood vessels can be clearly seen.

well be that the head would have a major problem identifying his perfusion apparatus as a proper substitute for his body. By movements of his eyebrows he can administer to himself some marijuana in case he feels the need.

This afternoon I spoke of just a few artificial organs. I did not talk with you about the artificial placenta or the artificial uterus. The artificial uterus is a subject to which Dr. Converse Peirce has devoted much study. Since it may become unpopular from the point of view of overpopulation, it might be better to talk to you about artificial spermatazoa which may be able to confuse the egg cell in the same way that the female screwworm fly is fooled by the irradiated male. I have not talked to you about the art of computer graphics, which can, in drawings never touched by human hands, simulate the blood flow through artificial organs. I have not talked to you about the artificial anus, and only those in the audience who need one can appreciate how important this is going to be. I have not talked to you about artificial kidneys which will work by adsorption of materials from the blood rather than by dialysis. It is certainly a pity that I could not talk to you about artificial cells, which can protect active enzymes in their own environment and which offer hope for the victims of approximately 250 different kinds of enzyme deficiency diseases, to have permanent substitution of the enzyme they need. Yet, of all these different things I have mentioned, we will certainly witness much in the seventies.

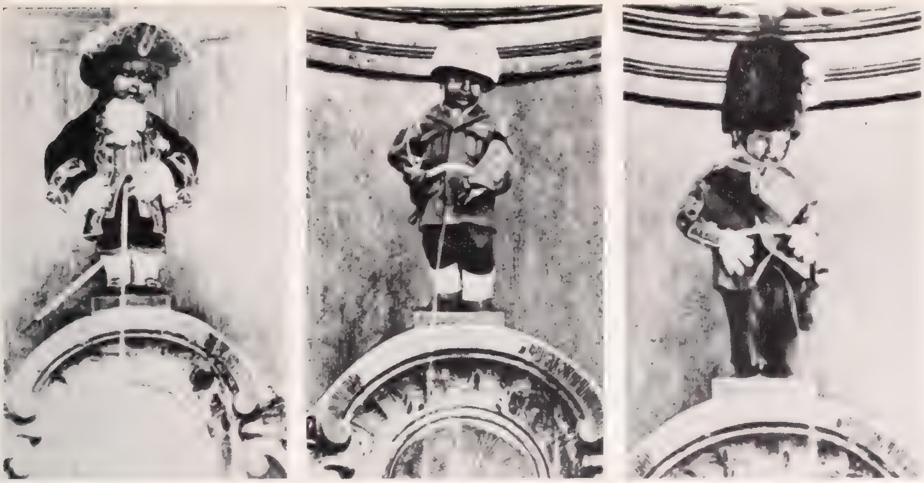

FIG. 7. The oldest citizen of Brussels.

I would like to close this presentation with the same picture which I showed here twenty-three years ago—a picture of the oldest citizen of the city of Brussels (Figure 6). Many honors have been bestowed upon him. You see him here in the uniforms of the Marquis de France, a member of the Canadian Military Police, and a member of the British Brigadier Guards. The picture reminds me, and should remind other artificial organists, that no matter how good an artificial organ we make, it will never work as well as this one.

From a Cat's Blood Pressure to a Toad's Bladder: Pharmacology and the Neurohypophysis—A Review

PETER J. BENTLEY, PH.D.

Introduction

The first description of the pituitary gland is usually ascribed to Galen, but it is only during this century, about 1800 years later, that its true functions have begun to be understood. The two principal regions of the gland are the adenohypophysis (anterior lobe) and the neurohypophysis. Embryologically these are different tissues. The adenohypophysis is ectodermal, derived from the roof of the mouth. On the other hand, the neurohypophysis is neural in origin, and is formed as a downgrowth of the brain with which it continues to maintain close connections. The neurohypophysis is not vital for life in man, but its activities assists our general comfort and well being. Thus, a deficiency of the neurohypophysial antidiuretic hormone (ADH, vasopressin) results in the formation of excessive volumes of urine (diabetes insipidus), a condition which may be inconvenient during the day and disturb sleep at night. However, providing that adequate drinking water is available and the thirst mechanism is functioning properly, life will not be endangered. More serious in man are the conditions in which excessive amounts of this hormone are secreted (inappropriate secretion of ADH, Schwartz-Bartter syndrome (1)) with a resulting hyponatremia and osmotic dilution of the body fluids. This can arise in a variety of situations (see Table I), the hormone itself originating either from a hypersecreting neurohypophysis, or from other tissue sites. The latter is a very interesting situation. Certain tumor tissues, notably oat-cell carcinoma of the bronchus, apparently may furnish additional ADH (2). The oxytocic, or uterotonic, action of the neurohypophysial hormone oxytocin, appears to assist uterine contractions during parturition and also "milk let-down" during lactation (galactobolic effect). These effects also are not vital but may facilitate normal physiological functions. The uterotonic actions have received considerable obstetric attention and preparations of oxytocin may be used to initiate or assist labor, and prevent postpartum bleeding. Pharmacological preparations of ADH are used to help control diabetes insipidus resulting from a deficiency of this hormone. Such peptides may have a variety of other uses including: elevation of blood sugar (following overdosage with insulin), promotion of intestinal contractions, and vasoconstriction such as in bleeding esophageal varices. These later effects represent pharmacological responses to the hormones rather than reflecting any such physiological role.

Today we recognize that two distinct hormonal entities, vasopressin (ADH) and oxytocin, are normally secreted by the mammalian neurohypophysis.

From the Departments of Ophthalmology and Pharmacology, Mount Sinai School of Medicine of The City University of New York, N.Y. 10029.

TABLE I

Disorders in Which There Is a Syndrome Probably Resulting from Inappropriate Secretion or Aberrant Production of Antidiuretic Hormone

1. Malignant tumors
    - Carcinoma of the lung
    - Carcinoma of the duodenum
    - Carcinoma of the pancreas
    - Thymoma
2. Disorders involving the central nervous system
    - Meningitis
    - Head injuries
    - Brain abscess
    - Brain tumors
    - Encephalitis
    - Guillain-Barré syndrome
    - Acute intermittent porphyria
    - Subarachnoid hemorrhage
    - Miscellaneous
3. Diseases of the lung
    - Pneumonia
    - Tuberculosis
    - Cavitation (aspergillosis)
4. "Idiopathic"

Thanks largely to the work of Vincent du Vigneaud we are aware of the precise amino acid constitution of these peptide hormones, and they have been made available as chemically synthesized materials. However, it was more than fifty years from the original identification of their biological activity in the neurohypophysis until this information was available. Nevertheless, commercial preparations of these peptide hormones were marketed and were used by physicians since before the first world war.

The discovery of the presence of these peptide hormones, along with their diverse pharmacologic and physiologic actions, the mechanisms of their action, and the precise quantitative measurements of their activity mainly utilize classic pharmacologic procedures. The mercury manometer, isolated organ bath, and smoked-drum kymograph are still adequate for much of this work, though for reasons of convenience, wealth, and fashion more sophisticated instrumentation is often used. The elucidation of our knowledge of the neurohypophysis has been associated with many famous men, including two winners of the Nobel Prize. The account which follows uses the historical approach to describe the evolution of our knowledge about this gland. Even in pharmacology the lessons of history may be useful, both with respect to the strategy for future work and as an appreciation of the experimental approach dictated by use of currently available techniques. The pharmacologist's contribution to our knowledge of the neurohypophysis has remained relatively simple technically, and furnishes an excellent example of the benefits of a keen intellectual and analytic approach combined with measurements which today may be termed "tedious," but which were once called "hard work."

Vasopressor and Oxytocic Activities

The first indication that a biologic activity resided in the neurohypophysis was found in 1895 on the occasion when Oliver and Schafer (3), from University College, London, published their account of the effects of extracts of the suprarenal glands. The catecholamines present in the adrenals were characterized by their ability to increase the blood pressure of decerebrate cats. An addendum to this paper included an account of how an extract of the pituitary gland also exerted a pressor action. Three years later Howell (4) showed that this latter biological activity resided in the neural part of the gland. This effect, reflecting a peripheral vasoconstriction, has been found to occur widely in anesthetized mammals (cardiac reflexes abolish the rise in blood pressure of normal animals) and is the basis in both the British and U.S. Pharmacopoeia (BP and USP) for the quantitative estimation of the activity of such material. It does not appear that this effect of the glandular extract reflects such a physiologic role for the hormone. The bioassay of this hormonal activity utilizes the rise in blood pressure of certain animals. Responses following injections of unknown amounts of the active material are compared to those seen after injecting a known (standard) quantity. While cats were initially favored for such work, an assay using rats was later introduced by Landgrebe, Macauley, and Waring in 1946 (5). These rodents provide a cheaper, more convenient, and less hazardous method for assaying such hormones and this is, in addition, acceptable in the BP and USP.

In 1906, H. H. Dale (6), who was then working at the Wellcome Physiological Laboratories in England, published a classic paper "On Some Physiological Actions of Ergot." This description has provided much of the basic information for the analysis of the mechanism of action of adrenaline and the sympathetic nervous system. Dale showed that many actions of the catecholamines could be specifically blocked by ergotoxine. Included in this paper were some observations on the effects of injection of ox pituitary extracts into female cats. In addition to bringing about a rise in the blood pressure, contractions of the uterus were observed. The original kymograph smoked-drum record is shown in Figure 1 and presents the first demonstration of the oxytocic activity in such glandular extracts. A little later, in 1909, Dale (7) showed that this activity was confined to the neurohypophysis, and that the uteri of rabbits, rats, and guinea pigs also responded both in vivo and in vitro. The size of the contractions of the guinea pig uterus in vitro were subsequently used by Dale and Laidlaw in 1912 (8) as the basis for a bioassay to measure the amount of oxytocin activity present in such pituitary gland extracts. However, the guinea pig uterus has a number of disadvantages, one of the most prominent being the difficulty in obtaining animals which have uteri which contract predictably. In addition, guinea pig uteri, like those of most other mammals, also contract in response to histamine which is a common contaminant in the glandular extracts. Again the laboratory rat provided an alternative preparation which behaves more consistently and does not contract in response to histamine (9). This was adopted in the BP in 1953. Herring (10) in 1915 eulogized the rat uterus in vitro "and [it]

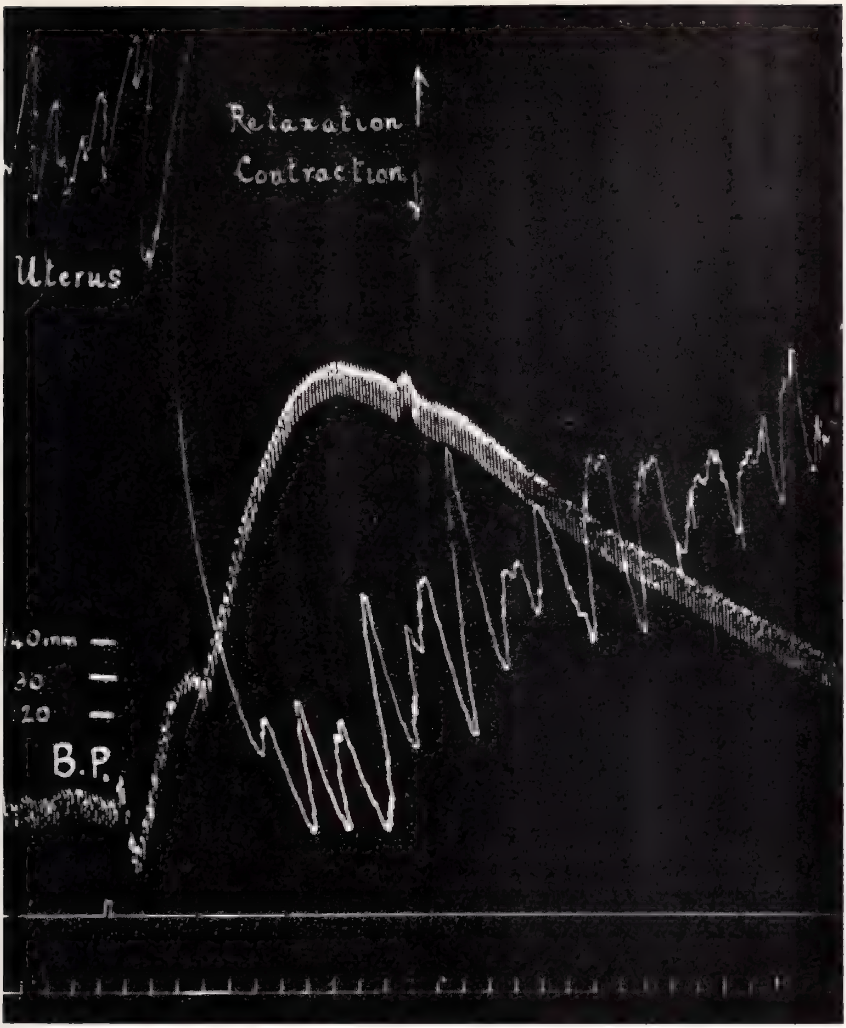

FIG. 1. Smoked-drum record of Dale's (1906) original experiments in which he described the oxytocic (uterotonic) action of ox postpituitary lobe extracts injected into a cat. The concomitant increase in blood pressure is also shown in the same record.

is in some respect more satisfactory [than the guinea pig uterus]" but his advice at that time went unheeded. It was later found that the nonmammalian homologue of the uterus—the oviduct of birds and reptiles—also may contract when exposed to such neurohypophysial extracts (11, 12), and this has afforded other assay procedures which, while not being of BP or USP quality, are occasionally useful in helping to identify naturally occurring hormone analogues from different species of animals.

The paper by H. H. Dale on "The Action of Extracts of the Posterior Pituitary Body" published in the *Biochemical Journal* in 1909 (7) is a fine example of the classic pharmacologic approach aimed at characterizing the activity in tissue extracts. It also serves as a reminder of the lucid logical approach of this great pharmacologist, who later won a Nobel Prize for his work on neural transmission. As already described, Dale substantiated his earlier work and demonstrated that the oxytocic effects of pituitary gland extracts were confined to the neurohypophysis. A powerful coronary vessel vasoconstriction, another important action of such extracts (which can be problematical when they are injected into man) was also demonstrated. This contrasted with the effects of adrenaline and afforded added information about the distinct properties of the two materials. He also showed that while the uterus of the rabbit rather uniquely constricted in response to both adrenaline and oxytocin, in other species adrenaline relaxed, while the pituitary extracts contracted, the uterus. To finally and unequivocally distinguish their actions he showed that ergotoxine blocks most effects of adrenaline (and sympathetic stimulation) but does not alter the pressor or oxytocic actions of the pituitary extracts. Dale considered the possibility that more than one substance was present in the posterior pituitary lobe extracts which could account for the diverse activities which were exhibited. He noted on certain occasions that oxytocic responses could be elicited in response to such injections while there was no change in the blood pressure. He cautiously stated, "It does not seem justifiable on this basis to conclude that the principles are different." He was, however, very close to uncovering evidence that, indeed, the active principles could be separated, for, while he showed that incubation with trypsin destroyed the vasopressor activity, he apparently did not test these extracts for oxytocic activity. It is now known that while trypsin can destroy the activity of vasopressin it leaves that of oxytocin unaltered. It was ten years before the separate integrity of these two activities was demonstrated. Dudley (13) in 1919 then showed that the oxytocic principle could be absorbed preferentially to the vasopressor activity into butyl alcohol. In 1909, Dale also showed that the vasopressor activity could be excreted in the urine and that immunity was not developed in a rabbit "treated for a month with increasing injections of the extract." Armed with a little hindsight this paper could be profitably read by many young and aspiring pharmacologists.

The Galactobolic and Antidiuretic Activities

A galactobolic or milk let-down effect of neurohypophysial extracts was described in 1910. Ott and Scott (14) who were working at the Medico-Chirurgical College of Philadelphia gave a brief but charming account of the increased rate of milk secretion from a nursing goat injected with posterior pituitary lobe extracts. These observations foreshadowed the hormonal role of oxytocin in assisting the release of milk from the mammary glands. Oxytocin thus became involved in reproductive physiology for a second time. Lactating mammals respond to different neurohypophysial peptides in a characteristic manner. Thus, vasopressin is about 6.5 times less effective than oxytocin. The galactobolic response is usually measured by recording changes in mammary duct pressure, and this can be used to characterize the neurohypophysial peptides. In addition, in suitably prepared rabbits and guinea pigs (15, 16), it affords the most sensitive assay method for detecting the small amounts of oxytocin which appear in the circulation during labor and suckling.

The most notable physiologic effect of the neurohypophysial secretions is to reduce urine flow by promoting water reabsorption from the renal tubule. In 1901 Magnus and Schafer (17) described a renal response to such pituitary extracts in anesthetized dogs. However, a pronounced and prolonged *increase* in urine flow was observed which subsequently led to the suggestion that the secretion may function as a *diuretic* (rather than an antidiuretic) hormone. This response was later used to help identify neurohypophysial activity and it was not until 1913 that von den Velden (18) showed that such extracts were antidiuretic when injected into man. Five years later von Hann (19) showed that diabetes insipidus may be associated with a disturbance in neurohypophysial function and the true antidiuretic nature of the secretion was recognized. The reason for the diuretic response is not clear but it is usually seen in anesthetized animals where the endogenous levels of ADH are already high. The role of the vascular effects of the hormone in this response have been considered by some but rejected by others. The diuretic effect is clearly a pharmacologic phenomenon and is a good illustration of the problems which may arise in animals under artificial experimental conditions. Extrapolations from pharmacology to physiology should be made cautiously. Bioassays for neurohypophysial secretions, utilizing the diuretic response were abandoned a long time ago. The antidiuretic response, however, offers the most sensitive method for detecting and measuring vasopressin. Trained unanesthetized dogs have been highly favored for this in many laboratories. Rats are usually more convenient, though normally not as cooperative. Their complicity can, nevertheless, be obtained. Ethyl alcohol has an admirable hypnotic effect and in addition reduces the rate of endogenous secretion of ADH (20). Drunken rats, which have previously been given a large dose of ethanol by stomach tube, respond to concentrations of ADH such as may appear in the circulation (21, 22, 23). The method has not the official status offered by the Pharmacopoeia's but is widely used for studies of the physiology of the neurohypophysis.

Vasopressor Activity in Birds

As illustrated by the observation of Dale that the rabbit uterus differs in its pharmacologic responses from that of other mammals, the pharmacologist frequently utilizes the biologic diversities present among animals in order to assist his studies. Different mammals often respond in dissimilar ways to pharmacologic agents so that it is not surprising to find that nonmammalian species may exhibit even more diverse responses. Paton and Watson showed in 1912 (24) that decapitated ducks exhibited a drop in blood pressure after the injection of postpituitary extracts. This reflects a peripheral vasodilatation and is in complete contrast to the vasoconstriction seen in mammals. They described their observations as "the peculiar results obtained by us with pituitrin." Shortly after Kamm and his group (25) in 1928 separated the vasopressor and oxytocin fractions from postpituitary lobe extracts, J. H. Gaddum (26) showed that in the domestic fowl the vasodepressor activity resided mainly with the oxytocic fraction. In 1939 J. M. Coon (27) of the University of Chicago utilized this response of the fowl in order to precisely assay the oxytocic activity in glandular extracts. In 1950 this procedure was officially adopted by the U.S. Pharmacopoeia as a bioassay for oxytocin, replacing the method of Dale and Laidlaw which used the guinea pig uterus. In 1953 the British Pharmacopoeia also adopted this method but the oxytocic action on the rat uterus also remained an acceptable procedure. It is very unlikely that such hormones have a physiologic vasodepressor action in birds. It is rather remarkable that such a response in chickens can be used to standardize preparations which are administered for their uterotonic activity in women.

The International Units of Activity

The necessity to use the bioassay procedures, such as have been described, was due to a lack of adequate knowledge about the molecular structure of the excitants and chemical methods for their measurement. We now know the chemical structure of these peptides. Dale and Laidlaw (8) in 1912 stated that "There seems to be no prospect at present of the control of its [the posthypophysial extracts] efficiency by chemical methods." This is still true today. Specific chemical measurements of these peptides do not appear to be feasible, although immunoassays are being developed. The availability today of pure peptides, such as vasopressin and oxytocin, provides us with material for "standard" preparations with which we may compare the activity of our "unknown" extracts. Results of bioassays can thus be expressed in terms of weight of the pure hormone. Until Du Vigneaud elucidated their structure and synthesized these peptides in the early 1950's (28, 29, 30, 31), even this was not possible. The creation of an artificial "standard" is a trick utilized by pharmacologists to take care of such situations when pure preparations of agonists are unavailable. Such standards may be made in an individual laboratory but this limits comparison with work carried out elsewhere. In the instance of the neurohypophysial activities an International Standard was specified in 1925 under the auspices of the League of Nations at Geneva. The International Units (IU) of oxytocic and vasopressor activity were defined as those present in 0.5 mg of an acetone-extracted and dried powder obtained from the fresh postpituitary lobes of cattle. However, it was found that the activity present in different batches of ox postpituitary lobes differed somewhat, so that a single standard, from which small samples could be dispensed, was made. This was done in 1935, again under the patronage of the League of Nations, and it was stored at the National Institute for Medical Research at Mill Hill in London. The second international standard succeeded the first in 1942 and a third, this time administered by the World Health Organization, in 1957. This is still being used today. As synthetic neurohypophysial peptides are now readily available it seems logical to conclude that these may replace the dried animal glands. However, the synthetic material is not always as stable as the activity in the crude ox pituitary powder. We can, however, translate the activity of the ox pituitary extracts into terms of the pure peptides

A. VASOPRESSOR-ANTIDIURETIC PEPTIDES

1. Arginine vasopressin (most mammals)

Cys-Tyr-Phe-Gln-Asn-Cys-Pro-Arg-Gly-NH_2
1 2 3 4 5 6 7 8 9

2. Lysine vasopressin (pigs and their close relatives)

Cys-Tyr-Phe-Gln-Asn-Cys-Pro-Lys-Gly-NH_2

3. Arginine vasotocin (lower vertebrates)

Cys-Tyr-Ile-Gln-Asn-Cys-Pro-Arg-Gly-NH_2

B. NEUTRAL OXYTOCIN-LIKE PEPTIDES

1. Oxytocin (mammals, birds, some sharks and rays)

Cys-Tyr-Ile-Gln-Asn-Cys-Pro-Leu-Gly-NH_2

2. Mesotocin (8-isoleucine oxytocin) (reptiles, birds, amphibia, lungfish)

Cys-Tyr-Ile-Gln-Asn-Cys-Pro-Ile-Gly-NH_2

3. Isotocin (4-serine, 8-isoleucine oxytocin) (most bony fish)

Cys-Tyr-Ile-Ser-Asn-Cys-Pro-Ile-Gly-NH_2

4. Glumitocin (4-ser, 8-glutamine) (some sharks and rays)

Cys-Tyr-Ile-Ser-Asn-Cys-Pro-Gln-Gly-NH_2

FIG. 2. Amino acid sequences of the known active natural neurohypophysial principles.*

which are present in it: 2.5 μg of pure arginine-vasopressin and 2.2 μg of oxytocin are equivalent to one International Unit of the artificial standard.

Chemical Structure and Polymorphism of the Neurohypophysial Hormones

Du Vigneaud and his collaborators in 1953 (28, 30) described the structure of mammalian oxytocin and vasopressin. They were found to be nonopeptides which differed from each other by two amino acid substitutions. Oxytocin has isoleucine and leucine at positions 3 and 8 in the molecule while vasopressin, instead of these, has phenylalanine and arginine at these sites (Fig. 2). These two changes account for the contrasting biologic activities of these hormones. There is only a crossover of less than five percent in the oxytocic and vasopressor and antidiuretic activities in each peptide. Since the original synthesis of the mammalian hormones, 200 to 300 artificial analogues of these peptides have been synthesized and all exhibit characteristic spectra of biologic activities when they are tested on the various bioassay preparations which have been devised. This has furnished a mine of information regarding the structure activity relationships which so often hypnotize and pervert the pharmacologist. However, the results, at least as regards information about precisely how the hormone works, have been rather disappointing. We know for instance that a basic amino acid, like arginine at position 8, enhances the antidiuretic activity as compared with, for example, leucine in this position, but we really do not know exactly how it does this. A fundamentally important and interesting observation made by Du Vigneaud and his group (30) was that the vasopressin obtained from pig pituitaries differed in structure from that found in the ox and most other mammals including man. Pig vasopressin has lysine instead of arginine at position 8 in the peptide (Fig. 2). This indicated that a polymorphism existed in the structure of the neurohypophysial peptides and this was soon found to be quite extensive. The substitution of lysine for arginine in the vasopressin molecule changes the biologic activity, but only to a small extent. Thus, a synthetic lysine-vasopressin is widely used today to treat diabetes insipidus in man. This is normally present in the pig family and not in man but it has adequate antidiuretic activities and in pharmacologic preparations is far more stable than synthetic arginine-vasopressin.

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* In parentheses, their main distribution in vertebrates.

At the present time eight different neurohypophysial peptides have been identified in different vertebrates. These often exhibit widely different biologic activities which have aided their pharmacologic identification. At least two of these peptides (vasotocin and mesotocin) were synthesized in the laboratory before it was known that they occurred in nature. An early collaborator of Schafer, P. T. Herring, who worked at the University of Edinburgh and then at St. Andrews, appears to be the first person to display an academic interest in the occurrence of neurohypophysial peptides in vertebrates lower down the phyletic scale than mammals (10, 32, 33). He made extracts from the neurohypophyses of various species and subjected them to various pharmacologic tests, mostly involving the blood pressure response of cats. He found that extracts from the pituitaries of birds (the domestic fowl), certain bony fishes (the ling, John Dory, and cod), frogs and toads ("used in my practical classes") and reptiles (tortoises) increased the cat's blood pressure. A cartilaginous fish, the skate, provided a disquieting note. Such an activity could not be demonstrated in its pituitary "although [he says] the skate does yield a substance which acts energetically upon mammary secretion." The significance of the latter observation was apparently not appreciated at that time. The lack of vasopressor activity was taken to reflect the absence of neurohypophysial activity in the cartilaginous fishes, a finding correlated with the lack of the distinct pars nervosa which is seen in higher vertebrates. We are aware today that indeed there is little vasopressor activity in the pituitary glands of the skate but the prominent galactobolic effect reflects the pharmacologic activity of a structurally different neurohypophysial secretion.

Natural polymorphism in the structure of mammalian vasopressin and oxytocin was not seriously considered until much later than Herring's observations and despite pharmacologic evidence to the contrary was not generally accepted until Du Vigneaud identified lysine-vasopressin in the pigs. The original identification of a natural neurohypophysial hormone, differing in its structure and activity from mammalian oxytocin and vasopressin arose from measurements of biologic activity using a novel and exotic bioassay procedure. Brunn (34) in 1921 showed that when frogs, sitting in water, were injected with mammalian neurohypophysial extracts they gained weight as a result of water retention. In 1941 H. Heller (35) working in the Department of Pharmacology at Oxford designed a bioassay utilizing this response. Heller prepared extracts from the neurohypophyses of various vertebrates including frogs, the pigeon, and the cod. He assayed these extracts by conventional methods using the guinea pig uterus and the blood pressure of the cat. When he injected such standardized extracts from lower vertebrates into the frogs they gained weight far more readily than when injected with extracts with similar assayable pharmacologic activities made from a rat's pituitary. The pituitary gland extract from a frog containing 40 mU vasopressor and 40 mU oxytocin activity when injected into frogs resulted in a considerable increase in water accumulation and body weight. In order to mimic this effect with an extract made from mammalian pituitaries the equivalent of 800 mU had to be administered. Heller at that time concluded that "the possibility must therefore be envisaged that the posterior pituitary glands of different classes . . . of vertebrates elaborate a secretion which exhibits the same activities —but by some unknown modification of the molecule—contains them in different proportions." Nearly 20 years later it was found that the activity which Heller had described pharmacologically was in fact arginine-vasotocin, a molecule which is a combination of the ring structure of oxytocin and the side chain of arginine-vasopressin and exhibits some properties of each of the mammalian hormones (11, 36). Prior to this positive identification of vasotocin in lower vertebrates the molecule had been synthesized earlier by Katsoyannis and Du Vigneaud (37). This is often cited as an instance where a hormone was made in the laboratory before it had been identified in nature. In view of the pharmacologic observations of Heller this is only partly true.

At least five other naturally occurring structural analogues of mammalian oxytocin and vasopressin have since been identified in various groups of vertebrates. Pharmacologic procedures have played a major role in the identification of these, though ultimately chemical methods are used to elucidate and confirm their structure. Apart from the methods for bioassay which have already been described there are several others (Table II) which, although not up to the British or U.S. Pharmacopocia's standards, provide additional ways for characterization of such substances. These assays include measurements of water and sodium transfer across amphibian membranes, such as the frog and toad skin and urinary bladder, the contraction of the turtle and hen oviducts, alterations in the oxytocic effects on the rat uterus when magnesium is present or is excluded from the bathing media (Table II). The activities of the various materials can be measured using a variety of such assays and a "pharmacologic fingerprint" or "profile" can then be made. Such differences in the activity of a number of such peptides are shown in Table III.

The differences between several neurohypophysial secretions were initially

TABLE II

Bioassay Systems Which May Be Used to Measure the Activity and to Identify Neurohypophysial Peptides (For References see Fitzpatrick and Bentley (38))

	Natural peptide(s) which may be usefully assayed
Blood pressure ↑ (cats, dogs, rats)	Vasopressins, vasotocin
Blood pressure ↓ (fowl)	Oxytocin, mesotocin, isotocin
Uterus in vitro (guinea pig, rat)	Oxytocin, mesotocin, vasotocin, isotocin, glumitocin
Oviduct (turtle, fowl)	Vasotocin, distinguish lysine- and arg-vasopressin
Antidiuresis (rats, dogs, mice, rabbits, etc.)	Vasopressins, vasotocin
Milk let-down –galactobolic (guinea pigs, cats, rabbits) (also myoepithelial strips in vitro)	Oxytocin, mesotocin, oxytocin, vasotocin, glumitocin
Amphibian preparations	
"Water balance effect" (frogs, toads)	Vasotocin
Isolated skin (frogs, toads)	Vasotocin, identify isotocin
Isolated frog or toad urinary bladder (water movement—hydroosmotic)	Vasotocin, identify isotocin
Sodium transport (bladder)	Distinguish lys- and arg-vasopressin

uncovered using such pharmacologic criteria. After the chemists provided simple chromatographic methods for the separation of peptides it became feasible to routinely separate the different activities contained in extracts from the neurohypophysis. The mammalian hormones could thus be separated by paper chromatography (39) into a "slow moving" and a "fast moving" fraction. When the strips of papers were cut up, extracted, and tested pharmacologically it was found that the "slow moving" material corresponded to the vasopressin while the "fast moving" section exhibited the activity of oxytocin. In lower vertebrates the arginine-vasotocin was found to be "slow-moving," when assayed it exhibited both oxytocic and vasopressor activity, while the "fast moving" material was oxytocic but lacked a detectable pressor (or antidiuretic) action (36). The

TABLE III

Relative Pharmacologic Activities of Naturally Occurring Neurohypophysial Peptides (From Fitzpatrick and Bentley (38))

Hormone	IU/mg peptide		
	Antidiuretic (rat)	Uterus oxytocin (rat)	Mammary gland galactobolic (rat & guinea pig)
Arg^8-vasopressin (ADH)	400	20	70
Lys^8-vasopressin (ADH)	250	5	60
Arg^8-oxytocin (vasotocin)	186	139	100
Oxytocin	5	450	450
Ser^4-Ile^8-oxytocin (isotocin)	1	150	300
Ile^8-oxytocin (mesotocin)	1	289	328
Ser^4-Gln^8-oxytocin (glumitocin)	Low	8	?

corresponding "fast moving" materials from a wide range of vertebrates including bony fishes, frogs and toads, birds and reptiles exhibit such oxytocic activity and these have an R_f which is for practical purposes indistinguishable. At first it was thought most likely that this oxytocic material was identical with mammalian oxytocin but close pharmacologic examination of its properties indicated that this was not always so. The first indication that it may differ from oxytocin arose from an examination of an extract from the pituitaries of a bony fish, the pollock. While the "fast moving" material exhibited the expected oxytocic activity, when Heller, Pickering, Maetz, and Morel (40) tested its ability to increase sodium transport across the frog skin in vitro, it was about 20 times less active (unit for unit) than mammalian oxytocin. Further assays uncovered more and greater disparities, indicating that a new and distinct hormone was present. This material was shown by Acher (41) to differ from oxytocin by two amino acid substitutions; it has serine at position 4 and isoleucine at position 8. It was called ichthytocin or isotocin and occurs in most of the bony fishes.

A second instance where a pharmacologic assay provided a critical test leading to the recognition of another such oxytocin-like hormone was afforded by observations of Follett and Heller (42). They examined the activities of extracts from the pituitaries of various amphibians (frogs and toads) and lungfishes. In the instance of the "fast moving" chromatographic oxytocic material from such extracts the effects on water and sodium transport across the amphibians' membranes is not sufficiently different (in contrast to that in most bony fishes) from that of oxytocin for it to be readily distinguishable. However, the vasodepressor action on the blood pressure of the fowl provides an assay of sufficient accuracy where a difference can be detected. Follett and Heller found that when tested on the fowl blood pressure, material from the amphibians and lungfishes with activity equal to that of mammalian oxytocin as previously assayed on the rat uterus behaved differently. The "fast moving" oxytocic fraction from the lungfish and amphibians consistently assayed about 1.6 times more strongly in the fowl than that of bona fide oxytocin. At that time many synthetic analogues of the neurohypophysial peptides were available for comparison and Follett and Heller concluded that the pharmacologic properties of 8-isoleucine oxytocin (oxytocin has leucine in the 8 position) were consistent with those of the material they isolated. Acher (43) had currently been elucidating the chemical structure of such amphibian peptides and at about the same time he published his results which indeed showed the structure was the same as 8-isoleucine oxytocin which had been synthesized 3 years earlier (44). The new hormone was called mesotocin.

Genetics and the Neurohypophysis

The observed polymorphism in the chemcal structure of the neurohypophysial hormones ushered this gland into the realm of genetics. Systematic differences have also been observed in the ratios of the amounts of vasopressin: oxytocin stored in this tissue (see 45, 46). Thus, different mammalian groups exhibit broad differences. In man the ratio is about one-to-one, and apart from small but possibly significant variations it is about this in most mammals. Significant variations from this have been described by Ferguson and Heller (46) in marsupials (kangaroos, opossums, etc.) where the ratio is uniformly high and varies from 3:1 to 6:1 in Australian (as well as North American) representatives of this order. The tylopoda also exhibit such an elevated ratio in hormone levels; it is about 3:1 in both the camel and in the llama. Considering that the former are from Asia and the latter from South America, this is possibly a too remarkable coincidence to be due to chance and may be a systematic characteristic of this group. It is feasible that such differences in the chemical structure and storage of these hormones influence the animal's physiology but this is not apparent in nature. Possibly if a mutation results in a change which is too drastic, the animals do not survive in the wild. In the laboratory such changes have been identified. Some mice have been found to elaborate lysine-vasopressin (as the pigs do) rather than arginine-vasopressin of most other mice (47). In 1963 Valtin and Schroeder (48) identified a strain of laboratory rats (Brattleboro) which suffered from diabetes insipidus resulting from a deficiency in their ability to synthesize antidiuretic hormone (48, 49). It was found that rats which were homozygous for the condition formed no detectable antidiuretic hormone while heterozygotes formed reduced amounts. It seems likely that hereditary diabetes insipidus in man may have a similar basis and this could result from an inability to synthesize the hormone or even result from the substitution of another structural analogue lacking adequate antidiuretic activity. The identification of such differences in animals depends on the bioassay of the material present in the neurohypophysial tissue. Thus, a simple way of distinguishing arginine from lysine-vasopressin depends on the enhanced ability of the former analogue to promote sodium transport across the isolated toad urinary bladder (46), a somewhat exotic and imprecise assay, but effective for this purpose. Ferguson and Heller (46, 50) have recently found that lysine-vasopressin is not always the only antidiuretic hormone present in the pig family. In some species such as the warthog, the peccary, and the African giant forest hog arginine-vasopressin may also be present. The hippopotamus, a relative of the pigs, also exhibits such a genetic polymorphism and may contain both vasopressins (51). Thus, at least three neurohypophysial hormones may occur in a single animal. It appears that the homozygotes may exclusively possess either lysine- or sometimes arginine-vasopressin while the heterozygotes contain both peptides. The separate identification of each of these peptides is not simple technically, especially when they occur together. They must first be separated using chromatographic procedures and then be positively identified. This is most easily done pharmacologically by using the toad urinary bladder preparation as just described. Identification of genetic differences in the neurohypophysial peptides present in man is technically feasible using extracts from the plasma or urine but this does not appear to have been attempted.

Mechanism of Action of Neurohypophysial Hormones

A well rounded education about an endocrine hormone should include knowledge as to how it precisely works. This can be approached in several ways. When the chemical structure is known, and synthesis has been achieved the influence of changes in the molecular structure can be studied. Today some 300 synthetic analogues of the eight known naturally occurring neurohypophysial hormones have been made and their biological activities catalogued. Another approach is to examine the interactions of the hormones with pharmacological agents whose mechanisms and sites of action are better understood. The identification of biochemical changes which occur in the tissue during the response may be more difficult but are of definitive importance. The two main in vitro preparations available for such studies on the neurohypophysial peptides are from the mammalian uterus and the toad or frog urinary bladder. The former can be used to study the smooth-muscle oxytocic action and the latter serves as a model for the antidiuretic response.

It has been recognized for a long time that incubation of vasopressin with trypsin destroys its biological activity while that of both oxytocin and vasopressin are abolished when they are exposed to the action of thioglycollic acid. The enzyme disrupts the arginine or lysine in the molecule while the thiol breaks the disulphide bridge. However, the intimate reasons as to how such changes so profoundly affect the molecule's activity were not widely considered. In 1958 (52, 53) a novel in vitro preparation of the urinary bladder of toads was described which vigorously responded to neurohypophysial peptides. This tissue actively transports sodium from its mucosal (urinary) side to the serosal surface and is is osmotically permeable to water. Both these processes can be readily increased by antidiuretic hormone. In addition the sodium transport is increased by aldosterone. This tissue thus behaves in many respects like the mammalian renal tubule but offers an attractive simplicity in its morphological arrangement as it consists basically of a single layer of epithelial cells which can be studied in physiological saline solutions.

In 1960 I. L. Schwartz and H. Rasmussen (54, 55) described a series of investigations aimed at elucidating the mechanism of action of the antidiuretic hormone. They used the toad bladder preparation to study the change in osmotic permeability induced by this hormone. Substances such as n-ethylmaleimide, which interfere with SH groups on the bladder, blocked the response. This and other information involving the integrity of sulphydryl and disulphide bridges suggested the possibility that the S—S group in the hormone interacted with SH and S—S moieties at the receptor site. This conceivably could initiate a change in the molecular structure of the membrane and increase its permeability to water. Although it subsequently transpired that this was too simple an explanation (56), the questions asked and the experimental attack made constitute an important conceptual event in the chronicles of the neurohypophysial hormone. Since that time a variety of pharmacologic agents have been found to interfere (e.g. ethacrynic acid, valinomycin, adrenaline) with the action of vasopressin on the toad urinary bladder, but the most important and interesting agents tested are theophylline and adenosine, 3′,5′ monophosphate (cyclic AMP) which mimics its effects. Interest in the possible role of cyclic AMP in the action of neurohypophysial peptides arose from the observation of E. W.

Sutherland (57) that cyclic AMP may act as an intermediate of "second messenger" in the action of certain hormones including corticotrophin. Orloff and Handler in 1962 (58), showed that cyclic AMP mimicked the action of vasopressin on the toad bladder. In addition, it was known that xanthines, such as theophylline, could inhibit tissue phosphodiesterase which inactivates the nucleotide. Theophylline also mimicked the actions of vasopressin probably by inhibiting this enzyme. It was concluded that cyclic AMP may mediate the effects of vasopressin on the toad bladder (Fig. 3) and subsequent work has confirmed this and indicated that it also acts in this manner on the renal tubule. The subsequent steps, including the exact nature of the final effector response are unknown, though it has been speculated that small pores in the membrane enlarge and so let more water across the cell. Vasopressin appears to activate adenyl cyclase in the cell membrane and the receptor itself is probably closely associated with this enzyme. Whether or not adenyl cyclase is synonomous with the receptor is unknown. The beta-adrenergic actions of catecholamines are also associated with the activation of this enzyme and there has been much speculation that it may be their receptor site. It is interesting that there is increasing evidence that alpha-adrenergic agents may inhibit the activity of this enzyme and adrenaline also inhibits the action of vasopressin on the toad bladder (59). The initial receptor for vasopressin appears at least to be closely associated with adenyl cyclase.

Chronologically interest in the precise requirements and nature of the neurohypophysial peptide receptor somewhat preceded the elucidation of the role of a "second messenger" and the appreciation of the presence of a separate final "effector" mechanism. There appear to be several reasons for this, including the ready availability in the mid-1950's, of many structural analogues of these hormones. In addition the relationship between the receptor and effector as distinct entities was not generally appreciated, as it was not unreasonable to suppose they may be synonomous. It seemed likely at that time that a close examination of the precise agonistic structural requirements for different responses may give clues as to the hormones mechanism of action. Apart from

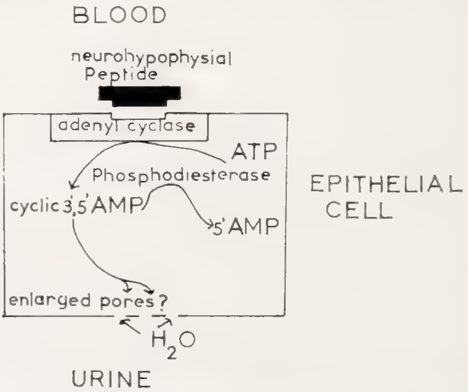

FIG. 3. Mechanism of action of neurohypophysial peptides on osmotic water movement.

these considerations the production of structural analogues was fostered for their possible commercial use in the hope of uncovering antagonists or peptides which emphasized one action of the hormone in contrast to another. Thus, addition of a methyl group to the phenolic residue on the tyrosine in such molecules reduced its activity and resulted in a molecule with some antagonistic actions especially on the rat's blood pressure and uterus (60, 61). Other molecules were produced which had an enhanced pressor activity and a much reduced antidiuretic effect or *vice versa* (62, 63). The potential uses of such antagonists or selectively vasopressor materials are obvious but they have not as yet gained general use. A lot of information about the structural requirements for a given effect has become available. Thus, it is well known that the antidiuretic action is enhanced by the presence of a basic amino acid, such as arginine or lysine at position 8 in such peptide molecules. The precise significance of such changes with respect to the receptor is not yet very clear. It has, however, been impressively demonstrated that the receptor requirements are very exact and fastidious ones. Current interpretations usually rest in the obscurity of the receptors "steric and electrical" requirements but a precise description of these is eagerly awaited. Whether they constitute an integral part of the adenyl cyclase molecule or have a separate identity which is linked to the enzyme is not clear.

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Sarcoma Botryoides of the Cervix Uteri:

A Case Report in a 75-Year-Old Woman

WILLIAM B. OBER, M.D.

Modern knowledge of sarcoma botryoides stems from the study by McFarland (1) who collated and reviewed reports of over 500 cases of urogenital sarcoma in both males and females, and described this tumor as a dysontogenetic neoplasm derived from the mesenchyme of the urogenital ridge. A later general review (2) of sarcoma botryoides attributed its histogenesis in females to mullerian mesenchyme. Citing reports of individual cases arising in the hymen (3) and anus (4), Salm (5) added that cloacal mesenchyme had the capacity to give rise to a morphologically indistinguishable tumor. Tumors of comparable gross and microscopic features have been described in the common bile duct (6, 7) and in the nasopharynx, middle ear, and maxillary antrum (8, 9). In a review of the histogenesis and taxonomy of mesenchymal sarcomas of the uterus (10), a class of tumor which is a special case in Stout's broad group of mesenchymoma (11), sarcoma botryoides was described as "the juvenile form" because it occurs predominantly in prepubescent girls and is rare after the age of 20.

The cervix uteri is a much less frequent site for the development of a botryoid sarcoma than the vagina. McFarland's (1) list of cases and his tabulation of data were too lengthy to be printed with his original publication and were deposited in the Library of the College of Physicians in Philadelphia. Analysis of his data reveals that of over 500 sarcomas in the urogenital region he classified 208 cases as botryoid. These comprise 72 examples arising in the vagina, 53 in the uterus, 39 in the bladder, and 44 in the prostate or urethra. Of the 53 uterine cases, only nine are specified as having arisen in the cervix uteri. It is, of course, self-evident that in a number of instances the observer cannot be certain of the precise site of origin of a bulky, complex polypoid tumor mass which has produced considerable local destruction.

Simpson (12) collected reports of 37 cases of sarcoma botryoides primary in the cervix uteri and added his own case. He divided them into two groups, 22 cases containing heterologous tissue elements and 16 cases which did not. In the former group, the average age at diagnosis was 32 years, with a range from 2¼ to 59 years. In the latter group, the average age at diagnosis was 22 years, with a range from one to 47 years. Of the entire 38 cases, only four patients were less than 15 years old and only three were over 50 years old. It appears that sarcoma botryoides arises in the cervix uteri chiefly during the years of active reproductive life, a contrast to origin in the vagina chiefly during infancy or childhood and in the corpus uteri chiefly after the menopause.

Only a few well documented cases of sarcoma botryoides primary in the cervix uteri have been reported since Simpson's survey, and these are listed with

From the Department of Pathology, Beth Israel Medical Center, New York, N.Y. 10003.

TABLE I

Sarcoma Botryoides of the Cervix Uteri—Cases Since 1950

Source	Age	Treatment*	Result	Heterologous tissue
Ferreira (1951)[13]	31 yr.	Total hysterectomy, BSO, X-ray	Died 18 months, Autopsied	Cartilage, No striated muscle
Dunster & Bennett (1953)[14]—Case 1	14 yr.	Total hysterectomy, BSO, Wide excision of parametrium, upper vagina, X-ray	Living & well 10 years	None
Dunster & Bennett (1953)[14]—Case 2	44 yr.	Same, No X-ray	Living & well 7 years	None
Richmond (1953)[15]	15 mo.	Total hysterectomy, Excision upper half vagina, broad ligs	Living & well, 6 years (Cited by Daniel *et al*[21])	None
Spademan *et al* (1953)[16]	58 yr.	Panhysterectomy, BSO Exc. upper ⅔ vagina, X-ray after recurrence	Died 5 months, Autopsied	None
Ober & Edgcomb (1954)[2] —Case 5	21 yr.	Hysterectomy, BSO	Died 3 years 8 months, Autopsied	Cartilage plus a few striated muscle cells
Taylor (1958)[17]	7 mo.	Hysterectomy, BSO	Died within 4 years	None
Taylor (1958)[17]	20 yr.	X-ray, then hysterectomy & BSO	Died within 4 years	Cartilage
Taylor (1958)[17]	38 yr.	Wertheim hysterectomy	Living & well 4½ years	Cartilage and striated muscle
Taylor (1958)[17]	48 yr.	Local excision, Radium X-ray	Living & well 7 years	Cartilage
Achari & Sahay (1963)[19]	60 yr.	Panhysterectomy	Living & well 8 months	None
Schade (1965)[19]	44 yr.	Radical hysterectomy LN dissection, Vaginal cuff removed	Living & well 3½ years	None
Ried (1968)[20]	10 wk.	Hysterectomy, Vaginal cuff, Ovaries preserved	Living & well, 15 months	None

*—Using the author's vocabulary

relevant data in Table I. As in any such survey, it is apparent that data is not complete on each case and that a number of cases were reported before the issue was determined. The present case is reported because it was detected in a woman at the age of 75 years, the oldest patient yet recorded with a primary sarcoma botryoides of the cervix, because of its unusual clinical course, and because it is determinate.

The two cases reported by Dunster and Bennett (14) each appeared as a single cervical polyp which recurred locally after simple excision; the case reported by Schade (19) was a bilobate polyp diagnosed as sarcoma botryoides, but no residual tumor was found in the hysterectomy specimen. Possibly survival in these three cases is related to the fact that the tumor was a simple polypoid sarcoma, largely exophytic. The four cases reported by Taylor (17) are cited in a general account of mesodermal mixed tumors, and details are not given fully.

All three autopsied cases showed extensive recurrent pelvic tumor with ureteral compression, involving bladder and rectum (13, 16), tumor thrombosis of the azygous vein with tumor extending into paravertebral muscle (13), and metastases to periaortic lymph nodes (16). Both hematogenous and lymphatic metastases occur.

Adding the present tabulation to Simpson's (12), the literature now contains

51 cases of sarcoma botryoides of the cervix, 27 containing heterologous elements, 24 with only homologous elements.

Case Report

A 75-year-old octoroon was admitted for the first time in April 1950, complaining of vaginal spotting for the past several months. Some tissue fragments had been extruded through the vaginal orifice. She had been aware of a mass which had prolapsed on occasion through the vagina. Physical examination revealed an obese, elderly woman with signs of moderately advanced but compensated arteriosclerotic and hypertensive heart disease. Several polypoid masses were seen arising from the posterior lip of the cervix; they prevented a complete speculum view of the cervix. Under anesthesia the uterus was felt to be small and freely movable; there were no adnexal masses. The cervical polyps were excised and their bases cauterized. Convalescence was uneventful, and the patient was discharged after four days.

She was admitted a second time in May 1951 after sustaining a fracture of the surgical neck of the right humerus after a fall. X-ray films showed a typical traumatic fracture with no evidence of metastatic tumor. She responded well to routine orthopedic measures.

She was readmitted in February 1953, complaining of a recurrent mass at the vaginal introitus, present for three months and associated with occasional spotting. Examination revealed a 3.5 cm polypoid mass attached to the cervix by a pedicle. Pelvic examination was otherwise unremarkable. Again, local excision and cauterization were carried out. Convalescence was uneventful, and she was discharged on the seventh day.

The fourth admission was in September 1955, the patient then 80 years old. She complained of recurrent vaginal discharge and spotting of 2–3 month duration. Examination disclosed a large cauliflower-like polyp occupying most of the vagina and seen to arise at about ten o'clock on the anterior lip of the cervix. A small polyp was seen at one o'clock just inside the external os. A small, raised, violaceous area was present on the posterior lip of the cervix. In addition, an ulcerated lesion 0.6 cm in diameter was found on the perineum at the vulvar fourchette; it had raised edges, and its crater was lined by a greenish slough. Under anesthesia, the uterus was small and freely movable; there were no adnexal masses. The polypoid lesions on the cervix were widely excised, and extensive cauterization and desiccation of the area was carried out. The perineal lesion was excised locally. Capsules containing radium were sewn to the cervix and removed two days later after a dose of 1440 r. Despite a borderline cardiovascular status, she withstood these procedures well and was discharged on the tenth day.

She was admitted a fifth time in January 1956 for wider excision of the vulvo-perineal lesion which had recurred and had extended toward the left labium majus. The lesion was excised widely and a cervical biopsy was done at the same time.

In April 1956, quadrant biopsies of the cervix were taken in the Outpatient

Department. She was examined again in May 1956. No lesions were seen on the vulva or cervix, but the uterus was now enlarged to the size of a 3-month pregnancy. She had no subjective complaints. Hysterectomy was advised but declined.

The patient remained asymptomatic until December 1957 when she developed abdominal distention and vomiting. A large abdomino-pelvic mass was present. It was presumed that she had intestinal obstruction and congestive heart failure. Conservative treatment relieved the intestinal obstruction, but cardiac failure became intractable. The abdomino-pelvic mass remained unchanged. She died in March 1958 at the age of 83, almost eight years after first exhibiting a polypoid tumor of the cervix uteri.

Pathologic Observations

Gross examination of the polypoid growths removed from the cervix in 1950, 1953, and 1955 showed multiple soft polypi ranging from 0.5 to 3.5 cm in greatest dimension, covered by sticky, mucinous fluid, varying on section from grayish-white to light tan with punctate reddish foci of hemorrhage. Microscopic examination showed the polypi to be covered in part by a thinned, atrophic, stratified squamous epithelium which was focally ulcerated. In many regions the complex polypoid architecture was outlined by compressed attenuated clefts lined by thin tongues of stratified squamous epithelium extending deeply into the substance of the tumor (Fig. 1). The polypi also incorporated scattered endocervical glands lined by non-neoplastic columnar epithelium (Fig. 2). Superficial patches of acute and chronic inflammatory exudate were present at the ulcerated surfaces, and aggregates of inflammatory cells were scattered throughout the stroma.

The stroma of the polypi was overtly sarcomatous, showing zones of increased cellularity resembling a "cambium layer" beneath the surface epithelium and around the included endocervical glands. Elsewhere, away from epithelial structures, cellularity was sparse and the stromal cells lay loosely dispersed in a myxomatous matrix. Closer examination of the stromal cells revealed considerable variation in size, shape, nuclear form, nuclear chromatin, and the arrangement of the stromal cells among themselves. Cellular pleomorphism was most pronounced in fields of greatest cellular density. The stromal cells exhibited unipolar, bipolar, and stellate (multipolar) shapes, bipolar forms being the most frequent (Fig. 3). The cell processes were delicate, indistinct, and formed a fibrillary matrix separated by a pallid myxoid ground substance. The nuclei varied from round to oval, some being indented, others irregular in contour. In some instances the nuclei were relatively large and hyperchromatic, often with prominent, even multiple nucleoli, but occasionally with crenated borders, condensed cytoplasm, and intranuclear vacuoles. In most fields the stromal cells were arranged at random with no regular orientation toward either the covering squamous epithelium nor the incorporated grandular elements. Mitotic figures were not frequent but were present. Multinucleated tumor cells and syncytial forms were extremely rare (Fig. 3). Heterologous elements were not identified in numerous sections; there was no evidence of carti-

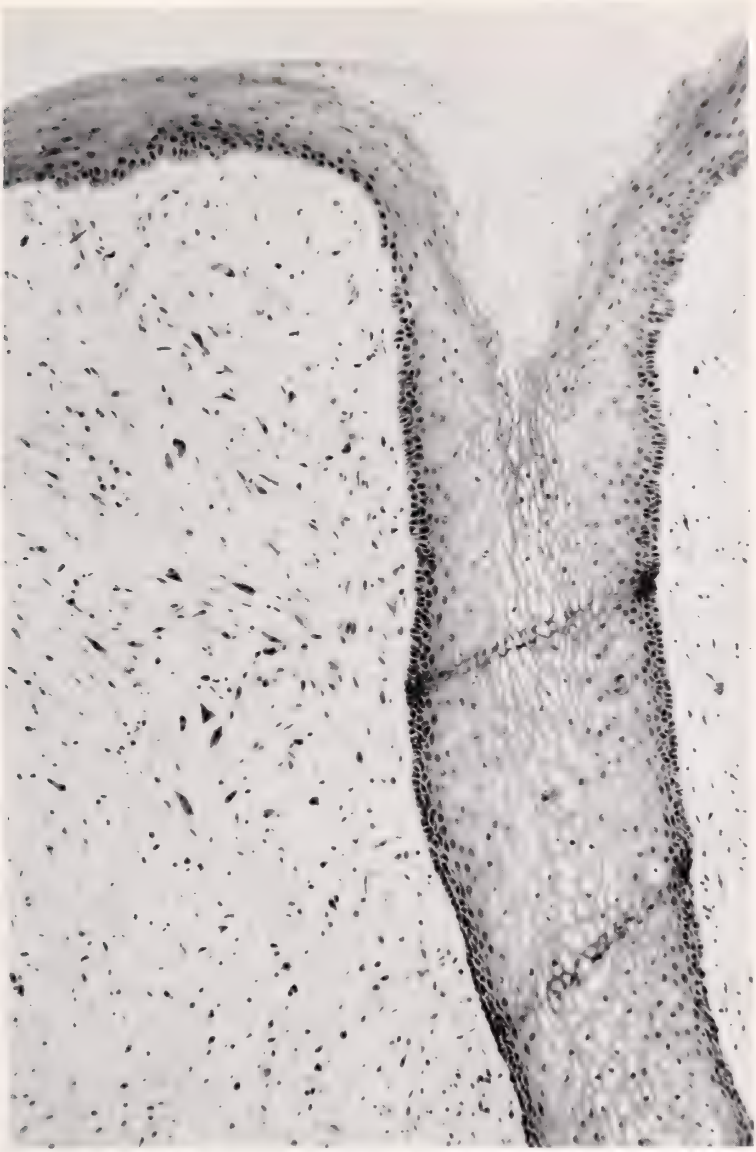

Fig. 1. Biopsy of cervical polyp (1950) showing an atrophic stratified squamous epithelium covering an edematous, myxoid stroma which contains many bipolar and stellate mesenchymal cells. A tongue of epithelium extends into a cleft within the polyp.

lage, bone, adipose tissue, or differentiation of tumor cells into myoblasts or rhabdomyoblasts. Only occasional cells exhibited a conspicuous volume of eosinophilic cytoplasm, but cross striations could not be demonstrated in them by a variety of special histologic methods. The neoplastic cells and myxoid ground substance merged almost imperceptibly into tissue identified as cervical wall. The pathological diagnosis was sarcoma botryoides.

Examination of the tissue removed from the vulvar fourchette in 1955 showed

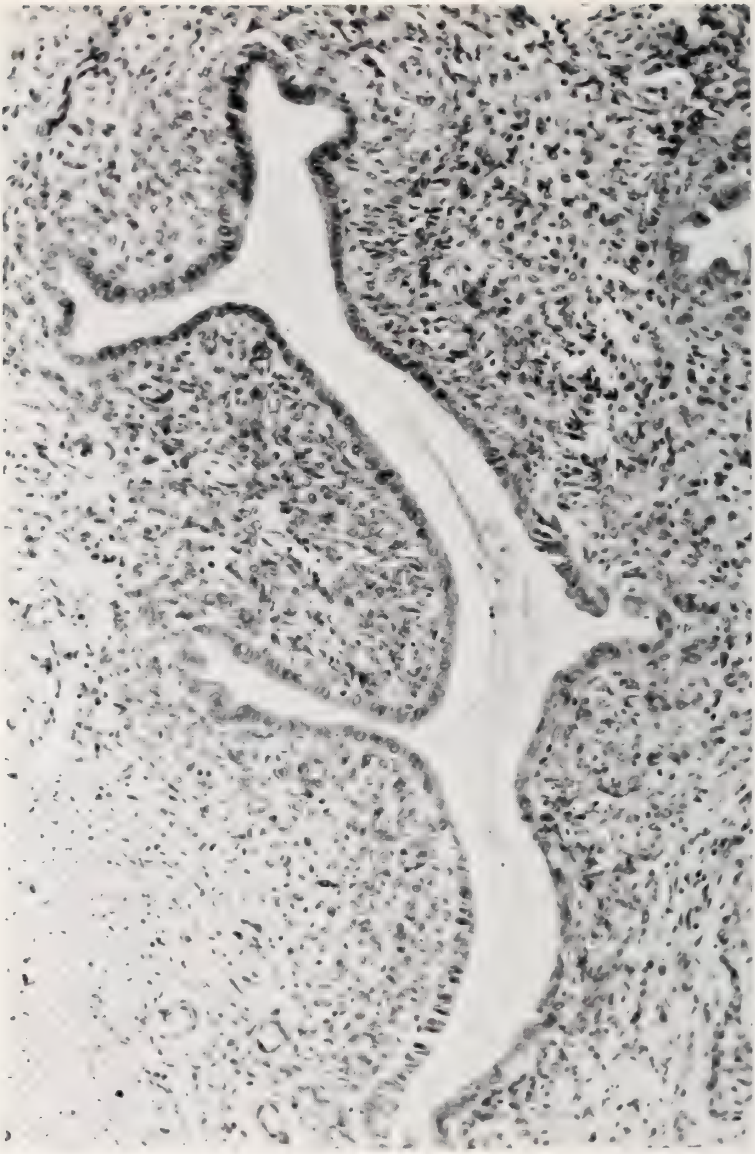

FIG. 2. Biopsy of cervical polyp (1953) showing an endocervical gland included in a somewhat noncellular zone of pleomorphic mesenchymal cells growing without pattern.

a moderately well differentiated squamous carcinoma invading subcutaneous tissue. Presumptive evidence of anatomically complete local excision was seen in sections prepared from the specimen obtained in January 1956. The cervical biopsy taken at that time and the quadrant biopsies taken in April 1956 showed only chronic inflammation.

Postmortem examination revealed the usual evidences of congestive cardiac failure complicating arteriosclerotic and hypertensive heart disease in an elderly

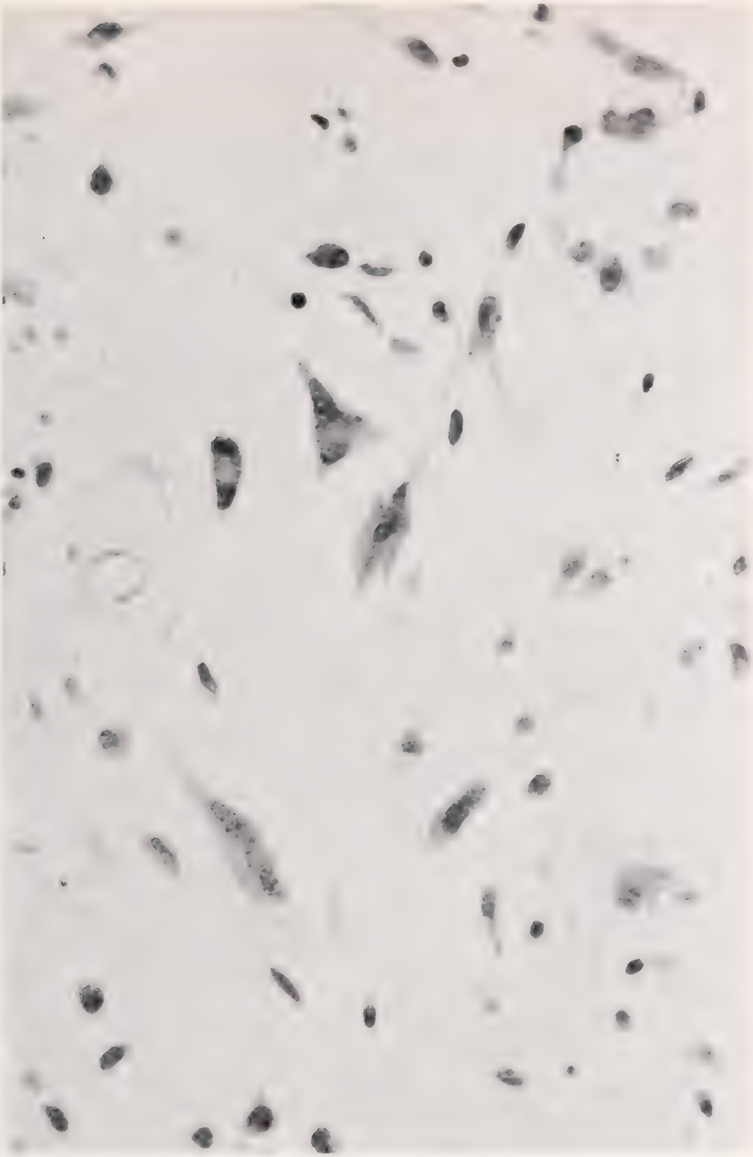

FIG. 3. Detail of Fig. 1, showing a few multinucleated and bizarre cell forms.

subject. There was no free fluid in the abdomen. The uterus was enlarged to the size of a full term pregnancy; its serosa was smooth and not adherent to omentum or any adjacent structure. The cervix was freely movable but indurated and replaced by tumor which, however, had not infiltrated into the paracervical or parametrial soft tissue. The Fallopian tubes and ovaries were atrophic. No secondary tumor deposits were found in inguinal or para-aortic lymph nodes, the retroperitoneal region, the liver, or any other parenchymatous organ.

The pelvic organs were removed and dissected separately. The cervical canal was occluded by firm, grayish-white tumor. On opening the uterus, a pyometra containing about 2 litres of thin, purulent fluid escaped, revealing a complex, multilobulated polypoid mass arising from the cervical wall and growing upward into the cavum uteri (Fig. 4). It was exophytic and had not infiltrated the cervical wall deeper than 1 cm. It did not involve either the bladder or rectum. Some of the polypi were soft and edematous; others were firmer and more fleshy. For the most part they were grayish-white, but the edematous ones were almost translucent, and an occasional polypoid structure was focally hemorrhagic. Microscopic examination of a number of sections prepared from the tumor at autopsy revealed a neoplasm identical in architecture and cell morphology to that seen in surgically removed portions. Again, no heterologous elements were identified. The tumor was composed of mesenchymal cells growing in a haphazard pattern. Only a few mitotic figures were found, and bizarre cell forms were infrequent. It was classified as a slowly growing, well differentiated sarcoma botryoides of the cervix uteri, homologous in cellular constitution.

Discussion

Customarily, sarcoma botryoides is considered a rapidly growing mesenchymal sarcoma which is only rarely amenable to radical surgical treatment. It is with surprise that one observes a case which remains confined to the cervix uteri from which it arose, remains localized for 8 years, and gives clinical evidence of its malignancy only by persistent local recurrence following local treatment. Two factors may have combined to modify the usual clinical course of this type of tumor in this individual: the advanced age of the patient and the relative maturity of the tumor cells. Although exceptions are not infrequent, it is a commonplace of oncology that tumors tend to grow more slowly in senescent subjects. Sarcoma botryoides usually develops in infants and growing children in whom equilibrium between cell death and cell regeneration has not been established. That a continuing, nonspecific stimulus for somatic cell growth furnishes a milieu in which rapid multiplication of neoplastic cells can be expected is a plausible hypothesis. A corollary to such a hypothesis is that, after such an equilibrium is established, tumor cell growth may be slower. In the present case, mitotic activity was low, and the tumor cells, though not fully matured, were not so immature as in most tumors of this class. With respect to this point, a distinction might be drawn between cell maturation, a nuclear function, and cell differentiation (or specialization), a cytoplasmic function. In this tumor the nuclei displayed relatively mature morphologic features, but there was no substantive evidence of cytoplasmic specialization. Yet, if one attempts to apply this argument to the presence or absence of heterologous tissue elements, i.e. visible evidence of cytoplasmic specialization, it fails to furnish a criterion from which the behavior of the tumor can be predicted or the outcome of the case anticipated.

Daniel et al (21) have listed seven cases of survival for five years or more in sarcoma botryoides of the vagina. (Their enumeration includes Richmond's

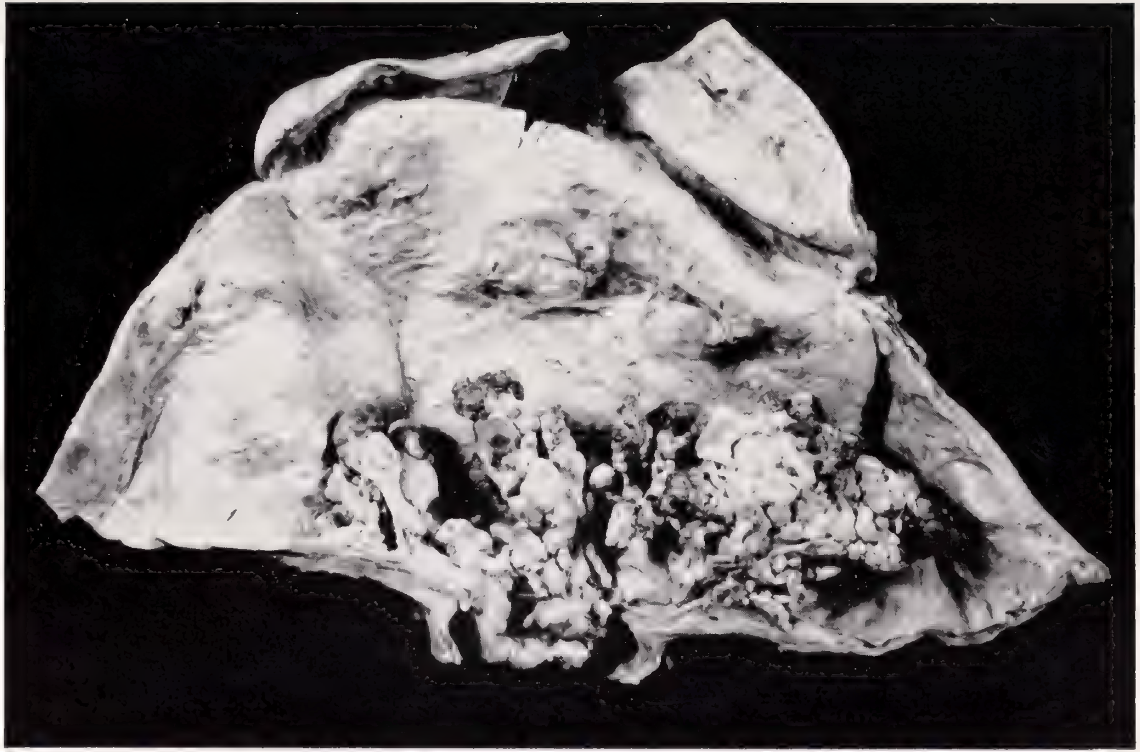

FIG. 4. Uterus at autopsy showing a complex polypoid growth arising from the cervix and extending into the cavum uteri. The uterus had been distended and its wall thinned by pyometra secondary to obstruction of the endocervical canal by tumor.

case (15), which arose in the cervix.) To this number must be added two children, reported by Sutow et al (22) in a survey of childhood rhabdomyosarcoma, who survived more than five years with vaginal sarcoma botryoides, albeit anamnestic details and methods of treatment are not recorded. Survival time was recorded in 28 of the 38 cases of cervical sarcoma botryoides reported by Simpson (12); only two patients survived more than five years, one a 25-year-old woman who succumbed after seven years, the other a 59-year-old woman living and well six years after hysterectomy, both cases dating from the first decade of this century. Of the 13 cases recorded since 1950, summarized in Table I, five died within five years of their disease, and three cases were reported before long-term survival could be gauged. Of the five patients surviving 4½ years or more, the two cited by Dunster and Bennett (14) are atypical, having presented as single polyps. Their report does not furnish histologic details and is open to the question raised by Norris and Taylor (23), who describe a number of vaginal polyps with cellular atypia resembling sarcoma botryoides but which pursued a benign course. Applying the most rigid criteria to the present series, only Richmond's case (15) and the two cited by Taylor (17), albeit without full details, can claim prolonged survival. The preferred method of treatment is extensive pelvic surgery, reinforcing the maxim that the anatomic extent of tumor at the time definitive therapy is instituted is the decisive factor, and that details of cell morphology and speculations about cell maturation and specialization are of only secondary importance in practical management.

Possibly, a word may be said about terminology. Admittedly, the vocabulary of oncologic taxonomy is unsatisfactory both as an exercise in language and as an epiphany of biologic truth. In recent years there has been an increasing tendency to label specimens which a past generation would unhesitatingly call sarcoma botryoides as "embryonal rhabdomyosarcoma." It may be legitimate to attack the term "sarcoma botryoides" as merely a term of gross description, denoting that these complex polypoid tumor often resemble a bunch of grapes, but that other mesenchymal sarcomas of comparable cell composition and presumably identical histogenesis do not assume the gross botryoid form. The distinction between botryoid and nonbotryoid mesenchymal sarcomas of the female genital tract may be purely a fortuitous function in which tumors growing outward into an open space are free to assume this gross configuration whereas infiltrative tumors do not. One can always fuse the concept of histogenesis with gross appearance and develop the term "mesenchymal sarcoma, botryoid type," a label which is clear in both clinical and pathological implications. But to supplant a time-honored term which at least affords a connotation of the gross clinical appearance of a tumor in favor of such a neologism as "embryonal rhabdomyosarcoma" flies in the face of reason. Not only is cartilage a more frequent heterologous tissue element, but identifiable rhabdomyoblasts are found only in a minority of botryoid sarcomas and, when present, usually constitute only a trivial proportion of the cell population. Salm (5) considers the occurrence of rhabdomyoblasts as "aberrant differentiation." To apply a new label to a familiar tumor may be justified if the new term adds to our understanding of the distinguishing features of that tumor, but when it is based upon a minority element, it seems as much of a solecism as to define a nation in terms of an ethnic or linguistic minority. However, this is neither the first nor the last occasion when a polysyllabic term of Greek derivation will be developed to mask our ignorance.

Summary

A case is reported of sarcoma botryoides arising in the cervix of a 75-year-old woman, the oldest patient yet reported to develop this tumor in this location. The tumor persisted locally, giving rise to two overt clinical recurrences. It was exophytic, slowly growing, and well differentiated. Heterologous tissue elements were not present. The tumor was present at autopsy, having remained confined to the cervix for eight years without metastasis. Its relative indolence is explained by taking into account the patient's advanced age and the relative maturity of the tumor cells. An intercurrent, unrelated squamous carcinoma of the vulva developed during the course of observation and was treated by complete local excision.

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Clinical and Immunologic Observations in Hypergammaglobulinemic Purpura

J. DONALD CAPRA, M.D.

The syndrome of hypergammaglobulinemic purpura was first described by Waldenström in 1943 (1). The patients exhibited recurrent purpura of the lower extremities, particularly after exercise, and an elevated serum globulin level. Despite the fact that the number of reported cases is now over 100, the syndrome is still poorly understood and rarely recognized. The purpose of this article is to discuss the clinical manifestations of the disease, present some new observations on the γ globulin alterations in these patients' sera and, finally, in view of these findings, to discuss an approach to therapy.

Clinical Picture

The coexistence of purpura and hyperglobulinemia occurs in all age groups (2, 3). Typically the patient is a relatively young female (18–40) who has had symptoms for 2–5 years before seeking medical advice. Generally, the complaints are of purpura of the ankles which is provoked by prolonged standing, exercise or the wearing of constricting garments. The location is generally of the lower extremities and usually below the calves. In some cases the purpura extends to the thighs, occasionally to the abdomen and we have seen a few cases with purpura on the upper extremities as well. The purpura is usually symmetrical.

The lesions are generally induced by exercise, especially walking, running, or dancing. Carrying heavy objects can lead to lesions on the forearms. Early symptoms of burning and itching are common.

The rash is petechial but at times is so severe as to appear confluent. All the lesions are generally in the same stage of evolution. For several years the lesions may fade and leave no residual but after several attacks a maroon and/or brown pigmentation remains. Trophic changes generally do not occur in the skin.

Pathologically the changes include perivascular infiltration of small vessels in the dermis, with acute and chronic inflammatory cells with some spotty arteriolar necrosis. Red cells are found free in the dermis. Later mononuclear cells are found in the perivascular cuff. Iron accumulates in the macrophages and free in the dermis.

Laboratory Findings

Typically these patients have extensive bleeding and coagulation studies and all tests are normal. The only consistent findings have been an elevated erythrocyte sedimentation rate and hypergammaglobulinemia. This hypergam-

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From the Department of Microbiology, Mount Sinai School of Medicine of The City University of New York, N.Y. 10029.

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maglobulinemia has been termed "polyclonal" as it generally appears polydisperse on serum protein electrophoresis. In 1961 Kunkel and his coworkers noted "intermediate complexes" on analytical ultracentrifugation of the sera of three of these patients (4). Later it was noted that the sera of many of these patients had high titer latex agglutinating activity, but they generally had negative tests for rheumatoid factors utilizing the sheep cell agglutination test or the Ripley test (anti CD serum Ripley-coated Rh O+ cells). These latter two test systems generally measure 19S (γM) anti gamma globulins while the latex fixation test measures both 19S and 7S (γM and γG) anti-gamma globulins. These data were consistent with the idea that the intermediate complexes were the result of γG anti-gamma globulins and thus resembled the situation in some patients with rheumatoid arthritis. The amount of "intermediate complexes" was impressive, and it was thought that perhaps all of the hypergammaglobulinemia could be accounted for on this basis.

Recent Findings

We have recently had the opportunity to study the sera of 16 patients with the typical clinical syndrome of hypergammaglobulinemic purpura (5). Intermediate complexes were seen in all (see Figure 1).

Utilizing BDB-aggregated γ globulin (to render it insoluble) these anti-gamma globulins were absorbed out of each serum and the serum protein electro-phoretic patterns invariably returned to normal. This was strong evidence that the anti gamma globulin antibody was responsible for the bulk of the hypergammaglobulinemia.

By acid elution of the insoluble immuno-adsorbant after it has been mixed with the sera of these patients we were able to isolate, quantitate, and characterize this antibody. The amount of γG anti γ globulin removed from each serum was found to correlate with the amount of complexes seen on analytical ultracentrifugation. A striking finding was that the eluates from every patient

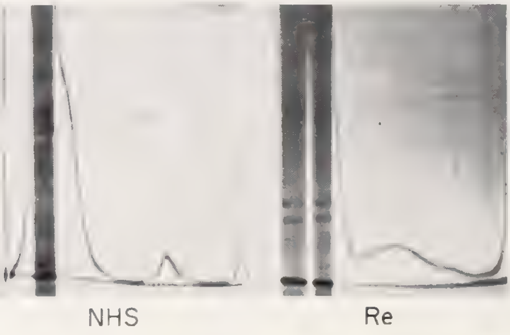

FIG. 1. Analytical ultracentrifugation of the serum from a patient with hypergammaglobulinemic purpura (right) with normal human serum included for reference (left). Both are diluted 1:1 with phosphate buffered saline pH 7.2. Photos taken 48 minutes after reaching 2/3 maximum speed of 52 640 rpm. Centrifugation is left to right. Note the large mound of "intermediate complexes" between the 7S and 19S peaks in the sera from the patient with purpura.

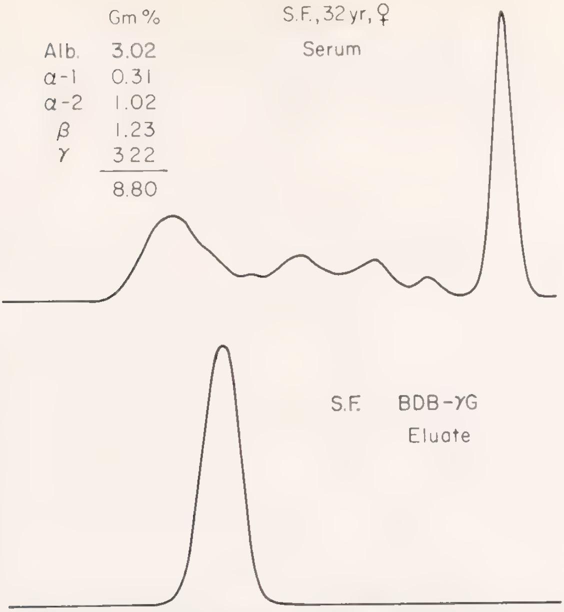

FIG. 2. Cellulose acetate electrophoresis of SF serum (top) and SF BDB-γG eluate (bottom). Note the polydisperse gamma globulin elevation which is typical of the electrophoretic patterns in this syndrome. The eluate migrates as a single component in the β-γ area.

had high titers of latex agglutinating activity documenting that all of the patients had γG anti γ globulins but that in some patients the latex fixation test was negative, presumably because the anti gamma globulins were fully saturated. These eluates reacted with aggregated γ globulin in precipitin tests and the precipitation could be inhibited by γG but not γA myeloma proteins.

Monoclonal Nature of Certain of the γG Anti γ Globulins

When tested under special conditions the sera and the eluates from some of these patients exhibited many of the properties of myeloma proteins in their degree of homogeneity. Cellulose acetate electrophoresis of whole serum does not generally reveal an M component (see Figure 2, top). However, a sharp band is observed in several sera on acid and acid-urea acrylamide gel electrophoresis. After isolation many of the eluates appear to migrate as M components on cellulose acetate electrophoresis (see Figure 2, bottom). Quantitative subgroup and genetic analysis on both whole serum and eluates suggest that most of these patients have in their sera γG anti γ globulins with restricted heterogeneity. Some of these eluates were prepared in large quantities. Individual antigenic specificity, light chain banding in acrylamide gels and sequence determinations confirmed their monoclonality (6).

One patient was encountered who had only a marginal increase in her gamma globulin level on cellulose acetate electrophoresis, but clinically had the typical syndrome of hypergammaglobulinemia purpura. On analytical ultracentrifugation intermediate complexes were seen and a monoclonal γG2 anti γ globulin was isolated from her serum. Thus, the possibility exists that there are several patients with hypergammaglobulinemic purpura who have normal γ globulin levels but who still have γG anti gamma globulins and as such should be included in this disease entity.

Treatment

Once we established that immune complexes were a constant feature of the disease, it seemed reasonable that an approach to therapy should involve the reduction in the level of these complexes in the serum. It should be noted that no treatment modality has had success with this disease entity in the past. Particularly, vitamins, radiotherapy, and steroids have been attempted and abandoned. We noted that two patients reported improvement in symptoms after a plasmaphoresis which was done in order to obtain large amounts of these complexes for sequence studies. Concomitant with their reported improvement, there were fewer complexes seen on analytical ultracentrifugation and a decrease in the amount of γG anti gamma globulin in their sera. A program was instituted in two patients for a single-unit plasmaphoresis each week and in a third patient for a 4-unit plasmaphoresis each month. All reported considerable improvement and an increase in exercise tolerance during a two-year followup. While spontaneous remissions are common in this disease it is unlikely that all three patients underwent spontaneous remissions. We have communicated this treatment modality to others, and they have had similar results.

Another potential mode of therapy is immunosuppressive drugs. We have been reluctant to administer these agents to patients with a supposedly benign disease, especially when it seems that simply doing a frequent plasmaphoresis will generally alleviate the symptoms.

Acknowledgement

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Method of Roentgen Demonstration of H-Type Tracheoesophageal Fistula

JOHN C. LEONIDAS, M.D.

Tracheoesophageal fistula without esophageal atresia (H-type) is relatively rare; it accounts for about four percent of all infants with fistulae between the trachea and esophagus (1, 2). Because continuity of the esophagus is preserved, the usual manifestations that lead to diagnosis of esophageal atresia within hours after birth are lacking. Diagnosis of H-type fistula may be delayed considerably, if the condition is unsuspected, and often demonstration of the fistula may be difficult despite strong clinical suspicion. Clinical manifestations include choking, coughing, and cyanosis with feeding (often more pronounced with liquid than solid foods); persistent or recurrent aspiration pneumonia, marked abdominal distension from air forced through the fistula into the stomach during expiration, excessive oropharyngeal mucus, and occasionally frothy stools (2–5). Diagnostic methods for demonstration and localization of the fistula are either endoscopic (tracheobronchoscopy and esophagoscopy) or radiologic (tracheography and esophagography). Contrast esophagography ("barium swallow") is the simplest and safest method to use and is highly successful, provided that proper technique is employed (4–6). The diagnosis of H-type tracheoesophageal fistula was recently established by this method in two newborn infants, and the diagnostic procedure will be described in detail to emphasize the significance of proper technique in making an early diagnosis.

Method of X-Ray Examination

Proper immobilization of the infant is essential. Both upper and lower extremities have to be restrained. The lower part of the patient's trunk and the lower extremities are firmly bound around an armboard attached posteriorly, so that any degree of obliquity of the body in relation to the x-ray beam may be achieved by simple rotation of the board (Fig. 1). A radio-opaque polyethylene nasogastric feeding tube of appropriate size (usually 8 French), with side holes at the distal end, is introduced through one of the nostrils down the esophagus and into the stomach. Aspiration of gastric content relieves the associated gastric distention characteristically present in patients with H-type fistulae. The patient is then placed in the straight lateral position, and under fluoroscopic control with image intensification, the distal end of the tube is positioned above the cardia. A very small amount of dilute barium is injected under careful fluoroscopic observation for connection between the esophagus and any part of the tracheobronchial tree. The tube is then withdrawn to a level 2–3 cm higher and the process is repeated. In this manner the entire length of the

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From the Department of Radiology, Mount Sinai School of Medicine of The City University of New York and The Mount Sinai Hospital, New York, N.Y. 10029.

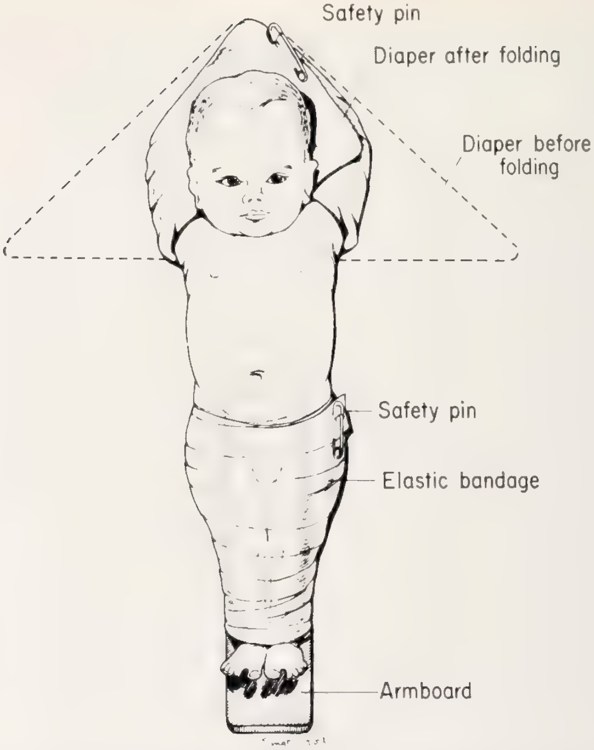

FIG. 1. Method of immobilization of infants. An armboard is placed behind both legs and an elastic bandage binds both legs to the armboard. A diaper, folded to form a triangle, is placed behind the shoulders. The right and left corners are folded over the arms and under the head as shown, then held in place with a safety pin.

esophagus up to the pharynx is injected with barium under fluoroscopic observation. Particular attention is paid to the upper esophagus, since most H-type fistulae are located at higher levels (usually at or above C2) than those associated with esophageal atresia (4, 5, 8). Opacification of the larynx and trachea during injections of barium in the lower pharynx and upper esophagus may create confusion in interpretation, since contrast may enter the airway either through an instantaneously filling high fistula or by regurgitation and aspiration through the glottis.

If a fistula is present, a small amount of contrast will enter it as the corresponding level of the esophagus is filled through the side holes of the nasogastric tube (Figs. 2 and 3). At the same time part of the tracheal lumen is opacified. The patient usually coughs, cries, and occasionally becomes cyanotic. With only minute amounts of barium injected each time, these signs are transient; the airway is cleared by coughing, and the patient soon appears quite comfortable. Nevertheless, close observation of the patient is strongly recommended. We keep the room relatively well illuminated during the procedure, since the image intensification coupled with closed-circuit television permits good perception in the light. We avoid using any recording device requiring additional radiation during fluoroscopic observation, unless a fistula is opacified or contrast is seen in the trachea. When this occurs a repeat injection of a small amount of barium is performed at exactly the same level while either 70 mm photofluorographic frames (at the rate of six per second) or a strip of cinefluorographic film are exposed. Videotape recording during fluoroscopy is highly desirable and may replace cinefluorography. Rapid sequential recording is necessary at present, since the fistula may fill for a very short time. Recording is particularly helpful when barium is being injected at or above the

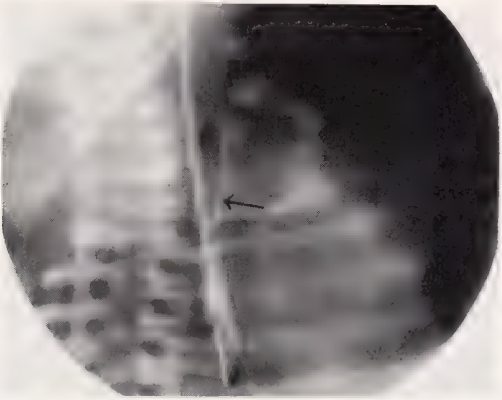

FIG. 2. Case 1. A fistula is visualized opacified by dilute barium at its esophageal attachment. It is at the level of the first rib and ascends to reach the posterior wall of the trachea.

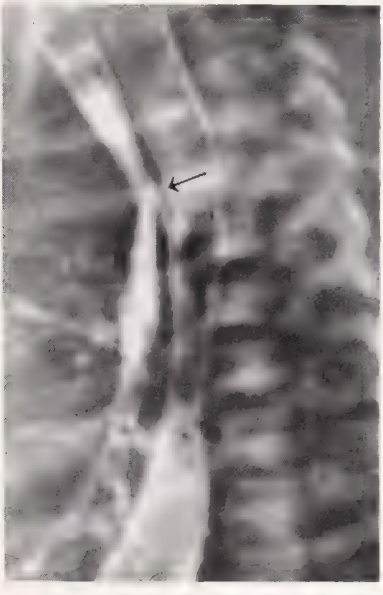

FIG. 3. Case 2. Tracheoesophageal fistula demonstrated after injection of a relatively large amount of barium. Filling of entire tracheobronchial tree. Fistula remains opacified after removal of tube. Note the typical appearance of all "H-type" fistulae, with tracheal end higher than esophageal (resembles more the letter N in the right lateral projection).

level of the cricopharyngeus. Replay and careful study of individual frames may differentiate between aspiration via the larynx and the presence of a high fistula. The diagnosis of a fistula is not made unless the fistula itself is demonstrated.

If no fistula is demonstrated in the lateral position the patient is turned into a prone oblique position (right side against the x-ray table, left hip elevated) and the series of injections repeated. Since fistulae extend from the anterior surface of the esophagus to the posterior surface of the trachea, the prone position may be advantageous in filling the fistula by gravity. In practice however the prone position may result in superimposition of the esophagus and trachea and obscure the exact point of communication. Esophageal motility is disturbed in the presence of a tracheoesophageal fistula, and observation of such changes should alert the radiologist (8). Deep inspiration following a period of crying may also be helpful in filling the fistula.

If no fistula is demonstrated with the maneuvers described, a bottle of flavored dilute barium is offered to the infant. Swallowing is observed and recorded by rapid 70 mm photofluorography or cinefluorography. In this manner any existing incoordination of swallowing accounting for aspiration will be demonstrated. At the end of the procedure frontal and lateral "overhead" chest radiographs are obtained, to exclude the presence of any trace of contrast in the tracheobronchial tree that might have escaped detection earlier.

An H-type fistula faintly opacified during injection of dilute barium into the upper esophagus is shown in Figure 2 (arrow). A small amount of contrast is noted in the trachea; it was cleared by coughing, and little contrast could be detected in the tracheobronchial tree at the end of the procedure. Only faint opacification of the fistula is adequate for diagnosis, and is safer for the patient. In the case of Figure 3 a more generous amout of barium was injected resulting in good filling of the fistula and trachea. This may cause temporary respiratory embarrassment. It was well tolerated by the patient in this case.

With few modifications, the method described is essentially that of Dunbar et al (6). The most important part of the procedure is the use of a catheter for injection of contrast. It allows control of the level of opacification of the esophagus with barium flowing towards the stomach, while the pharynx remains clear of contrast; this permits differentiation between tracheoesophageal communication through a fistula and aspiration via the larynx.

Discussion

Because H-type tracheoesophageal fistula is not a common congenital anomaly, experience with diagnostic procedures is necessarily limited. Some of the diagnostic methods proposed are clearly complicated when applied to newborn infants, often with respiratory function already compromised because of aspiration pneumonia. Thus tracheobronchoscopy and instillation of contrast into the airway further embarrass respiratory function, and both methods, as well as esophagoscopy, will require anesthesia or heavy sedation. Moncrief and Randolph (3) advocate surgical exploration when more conservative diagnostic methods have failed to establish the diagnosis. With our limited experience we would tend to agree with others (4–6) that properly performed barium esophagography is both simple and diagnostically accurate, and it is the procedure of choice for investigation of possible congenital tracheoesophageal communication.

As illustrated by Figures 2 and 3, most H-type fistulae are located at higher levels than fistulae associated with esophageal atresia (4, 5, 8). Occasionally the fistula actually appears as a laryngeal cleft, which is a high communication between larynx and pharynx. Endoscopic examination is more diagnostic in these cases (5) since roentgen examination will only indicate aspiration. The high position of H-type fistulae has an important surgical implication since a trans-cervical operative approach becomes feasible (4).

Barium is the contrast medium of choice for detection of H-type fistula by esophagography. Water-soluble iodinated contrast media (sodium and methyglucamine diatrizoate) are hyperosmolar substances, very dangerous when aspirated, causing pulmonary edema (6, 7). The use of oily propyliodone (Dionosil®) is not indicated since the high viscosity of this substance may preclude visualization of small fistulae. Dionosil® is being used in some departments at the onset of esophagography as a precaution against massive aspiration in case of a very wide communication (5). Injection of very small amounts of contrast medium under constant fluoroscopic control makes the difference between Dionosil® and barium insignificant (6).

Summary

Properly and carefully performed barium esophagography is probably the safest and most accurate diagnostic procedure for early detection and preoperative localization of H-type tracheoesophageal fistula. The roentgenographic technique is described in detail.

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Retractile Mesenteritis: A Case Report and a Review of the Literature

ARTHUR SICULAR, M.D. AND EDWARD B. GREENSPAN, M.D.

Retractile mesenteritis is a rare clinicopathologic entity first described in 1897 (1). Initially, the symptoms are abdominal pain, and, in extreme instances, complete intestinal obstruction. The following case is a unique example of the complete syndrome.

Case Report

D.P., a 78-year-old woman was admitted to The Mount Sinai Hospital with increasing constipation, increasing abdominal girth, intermittent nausea, and vomiting. Three months before, she had been hospitalized for severe cramp-like abdominal pain, occurring intermittently over a four-year period, accompanied by intermittent constipation unrelated to diet and associated with a recent weight loss. A roentgenogram taken at the time revealed a sliding hiatus hernia and scattered diverticulae of the sigmoid colon. It was thought that diverticulitis might explain the constipation and abdominal pain. Sixteen and eleven years earlier, the patient underwent bilateral mastectomies for carcinomas of the breast, without overt evidence of spread. Twelve-channel SMA reports were within the normal range except for albumin of 3.0 gm percent.

At the present admission she was emaciated and chronically ill, with pertinent findings limited to chest wall and abdomen. There was marked dehydration and marked abdominal distension. There was no lymphadenopathy or hepatosplenomegaly, and the rectal examination was negative. The abdomen was tympanitic, with slight epigastric tenderness. There were grade 1 varicosites in the legs, with good arterial pulsation; the deep reflexes of both legs were depressed. The white blood cell count was 6900; the differential count was normal; hemoglobin was 14.3 gm percent. Urinalysis revealed the specific gravity to be 1016, with a trace of albumin and occasional white blood cells. During the three days prior to her admission, the patient experienced excruciating intermittent abdominal pain unrelieved by occasional bowel movements. On the day of admission she had nausea and vomited a greenish fluid. A small nontender inguinal hernia was noted. Roentgenogram film of the abdomen revealed the small bowel to be markedly distended without colonic air. She was prepared for five days with Cantor intubation, which somewhat diminished the distension, but did not relieve what became a total low small bowel obstruction. On the fifth day, an exploratory operation was performed, revealing these findings: The small bowel was distended, the distension increasing from the jejunum towards the terminal ileum, and a 12 cm diameter of the small bowel was noted within two and one-half feet of the ileocecal valve. Distal to a point of obstruction, the small bowel was collapsed, as were the cecum and colon. Only a few quiescent sigmoid diverticulae were to be seen in the colon. The liver, spleen, stomach, pancreas, and base of the mesocolon were normal. There was a small but reducible hiatus hernia. The uterus was small and the ovaries were atrophic. There was a striking retraction and marked thickening of the base of the jejunoileal mesentery by a flat infiltrative process which expanded caudally to the edge of the mesoileum until it enveloped the ileum at a site three feet from the ileocecal valve. This mesentery was bluish-white, firm, and contiguous, but the ileal lymph nodes in this area were not involved. The ureters could not be seen through the process, which was of varying thickness within the distal mesentery. A laparotomy was performed, and specimens of the mesoileum and an ileal node were taken for biopsy: the proximal bowel was decompressed over the Cantor tube and a side-to-side ileocecal anastomosis was made. Approximately 2500 cc of fluid and an equal amount of air was aspirated from the proximal bowel during decompression. The patient's postoperative course was complicated by thrombophlebitis and a pulmonary infarction requiring heparinization and continuing anticoagulant therapy with Coumadin®. Esophagitis developed as a result of the prolonged Cantor intubation through a hiatus hernia. The esophagitis subsided on milk and alkali, and the patient was discharged from the hospital after a month.

Six months after surgery, she had regained 30 lb to reach her normal weight of 120 lbs. She was alert, active, and vigorously pursuing her normal activities. No abdominal masses were seen or palpated on abdominal, pelvic, or rectal examination. A repeat gastrointestinal series done prior to her last visit showed a normal esophagus and stomach with a hiatus hernia. The duodenum was normal, without fistula or ulceration. The jejunum was slightly dilated and shortened. The entire ileum was shortened. Several loops of distal ileum were also somewhat agglutinated and distorted. (See Figure 1.) One barium swallow filled the entire small bowel. Barium enema of the colon freely filled the colon from rectum to cecum and demonstrated a side-to-side ileocecal anastomosis and a narrow terminal ileum, with agglutination, distortion, and irregularity of mucosal folds.

Pathology Report

The specimen taken from the ileal mesentery on May 18, 1970 was a wedge of firm white tissue showing fibrosis without evidence of neoplasm or purulent inflammation. (See Figure 2.) The fibrofatty tissue showed increased capillaries infiltrated by a moderate number of lymphocytes, plasmacytes, histiocytes, and a few neutrophils. A lymph node from the ileal mesentery showed normal structure, intact capsule and germinal centers. Diagnosis was chronic mesenteritis with fibrosis.

Conclusion

Retractile mesenteritis is an unusual disorder of the mesentery. Clinically it varies in a spectrum from acute abdominal pain and nausea with chronic obstipation and constipation, to insidiously developing total intestinal obstruction. The roentgen characteristics in the small intestine are variable and

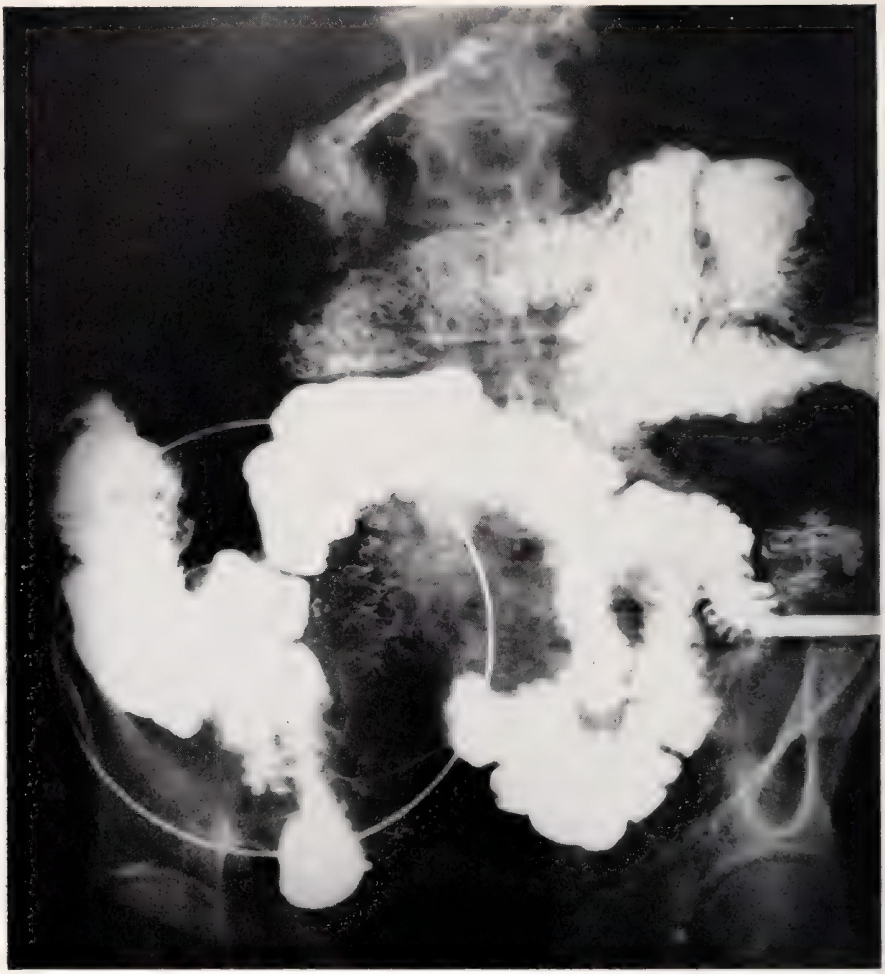

FIG. 1. Small bowel examination reveals an ileoascending colostomy side-to-side. There is a large mass 8 x 10 cm overlying the body L5 and the sacrum. There is minimal dilatation of the intestinal loops in the region. The bowel surrounding the mass is shirred with pleating of the valvulae conniventes. The findings are consistent with a fibrotic process in the mesentery (by R. H. Marshak, M. D.)

suggestive, but not diagnostic of the condition. Surgical procedures are limited to biopsy for establishment of the diagnosis and possible underlying disease, with appropriate short-circuiting of obstructions or lysis of angulating adhesions. Etiology is complex and pathogenesis unknown. Prognosis of the syndrome is uniformly surprisingly good.

Pathologic entities established in three groups include: 1) an acute, fatty, infiltrative picture. 2) subacute lipodystrophy with foreign body giant cell formation, macrophage infiltration, and plasma cell involvement. 3) a chronic form associated with fibrosis, fibrocytes, collagenization, and some round cell infiltration. The gross pathology creates a thickened, infiltrated, placque-like

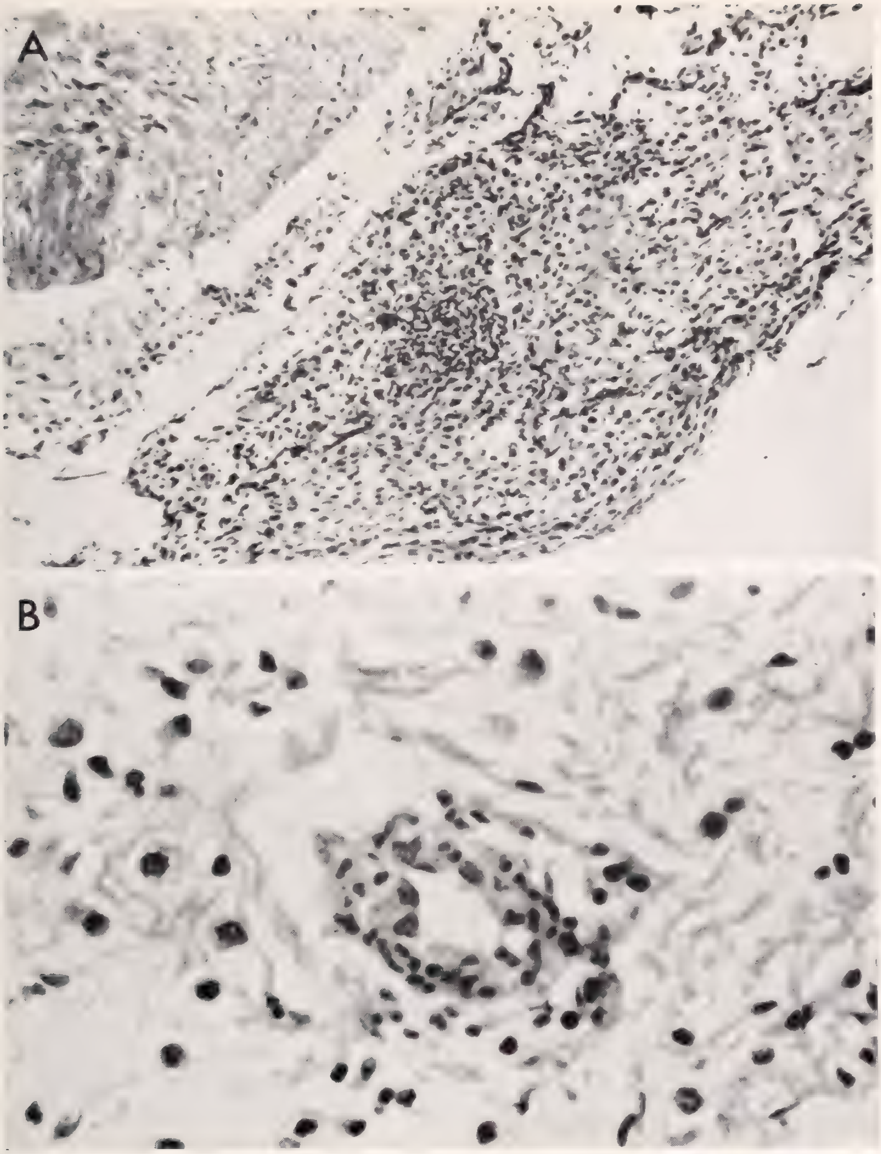

FIG. 2a. Gross picture: The mesenteric biopsy is a white, firm wedge. The outer surface is dull. The cut surface is smooth and solid. 2b. Microscopic examination shows moderately cellular fibrous collagenous tissue infiltrated by lymphocytes, plasma cells, and some neutrophils. There are many small vessels, some of which show acute inflammation in the wall and the surrounding connective tissue without acute fibrinoid necrosis. (by Peter Teng, M.D.)

involvement of the ileal mesenteric border to envelop and obstruct ileum or colon. The degree and acuteness of the process determine the exhibition of the corresponding phase of the clinical syndrome, which is limited to an abdominal syndrome without systemic manifestation.

Discussion

Retractile mesenteritis is a rare disorder which involves shortening, thickening, and infiltration of the small bowel mesentery. The infiltrate may be fat, inflammatory tissue or fibrosis. All of these result in unusual intestinal angulation, obstruction, or pain, and in extreme cases such as this, go on to an intestinal obstruction related to kinking or actual encircling focal involvement. The first report of this entity was made by Riedel in 1897 (2). The first case review and establishment of the entity as a clinical syndrome has been credited to Jura who reported a series of more than 20 cases (3). The ages of patients with the syndrome range from eight to eighty years (4).

The gross picture at laparotomy is rather characteristic and striking. There is a flat, truncated, pyramidal involvement of the small bowel mesentery which is wide, firm, pale, and grey-to-opalescent. The process has been described as wide as 10 cm at its base. In our case, 8 cm was the maximal width. There is irregular extension around and towards the antimesenteric border, with plaque and nodular involvement being noted. The lymph nodes do not appear to be involved in the process. There is no free fluid or evidence of lymphatic channel obstruction, and the process does not extend to the solid viscera.

The microscopic pathology is reported in three major subgroups. The initial mesenteric infiltration may be of fat cells, macrophages, and round cells. A second pattern involves the presence of polymorphonuclear cells, giant cells, scattered fibrosis, and fat degeneration or dystrophy. A third type, as in the case summary above, involves a desmoplastic reaction with fibrocytes, excessive collagenization, and scattered round cell infiltration. The lymph nodes do not appear to be abnormal. Pathologic entities which may produce this clinical picture include multiple lipomata, lymphosarcoma, mesenteric metastatic signet cell carcinoma, retroperitoneal fibrosis associated with methysergide (sancert), sarcoma, carcinoid, metastatic carcinoma to the mesentery and Whipple's lipodystrophy (5). Attempts to duplicate the syndrome (6) have been made by direct mesenteric injection of viable B. coli or tuberculin. In rabbits, a picture of injury reaction and degeneration with inflammatory infiltration, fat necrosis, and giant cell reaction leading to fibrosis has been produced, which is similar to that described in many reports (7). Approximately 50 percent of the cases reported have had previous surgery not immediately related to the onset of the syndrome (6). Ten percent of the cases reported have had Gardner's syndrome of multiple small bowel tumors and soft tissue tumors (8). The x-ray picture is summarized in an atlas by Marshak (9). "The esophagus and stomach are unremarkable. There may be compression or distortion of the distal duodenum near the Ligament of Treitz. Separation of small bowel loops, with fixation of patterns and bizarre kinking and angulation may be noted, without evidence of mucosal ulceration or fistula. Mild distention or huge distention and small or large bowel obstruction complete the picture. An indirect sign is the rapid and complete filling of the small bowel loops by a relatively small amount of barium, suggesting the retraction and shortening of the mesentery."

The specific therapy of the syndrome is unknown. Surgical treatment when necessary is limited to bypass of obstructed areas or lysis of angulating adhesions. The prognosis following these simple procedures is surprisingly good. Biopsy will usually rule out the differential diagnostic etiologic possibilities.

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Significance of Delayed or Prolonged Opacification of the Renal Arterial System

HAROLD A. MITTY, M.D. AND MURRAY G. BARON, M.D.

Delayed or prolonged opacification of the renal arterial system when observed during the course of aortography or selective renal angiography is indicative of significant pathology. Since serial filming over a known period of time is used during angiography, one may make observations related to aberrations of blood flow. The finding of delayed or prolonged opacification of the renal arterial system can be the result of impaired arterial filling, often associated with flow through collaterals, or slow washout of the contrast material.

Technique

The duration of renal arterial opacification will vary somewhat depending on angiographic technique, particularly injection rate and catheter placement. For this reason, abnormalities related to delayed or prolonged renal arterial opacification are most often apparent when both kidneys or segments of the same kidney are compared. Aortography is performed with a green Kifa catheter having four side holes that is placed at the midportion of the first lumbar vertebrae. Forty cc of contrast material* is injected at a pressure of 400 pounds per square inch with a Cordis injector. Selective renal artery injections are made through a green Kifa catheter having no side holes. A volume of 7 cc of contrast material* is injected by hand. Filming rates are recorded so that the appearance times of the various angiographic phases may be compared from patient to patient.

When delayed or prolonged renal arterial opacification is demonstrated, the causes fall into three categories: 1. Those cases due to major or segmental arterial lesions which obstruct or alter vascular dynamics, 2. Diffuse parenchymal processes which cause significant loss of renal substance and/or obliterate the peripheral renal vascular bed, and 3. Venous obstruction.

Arterial Lesions

From our experience as well as that of published reports (1, 2, 3), a stenotic lesion is more apt to be functionally significant if there is poststenotic dilatation, collateral flow, or slow filling beyond the lesion. These findings often coexist in the same patient. For example, a stenosis may be severe enough to restrict flow and result in poststenotic dilatation. The eddy currents set up beyond the stenosis lead to inefficient flow and prolonged opacification of the poststenotic arterial tree. In addition, if collateral flow occurs around the stenosis, this more circuitous route results in later filling of the poststenotic segment (4).

From the Department of Radiology of The Mount Sinai Hospital and Mount Sinai School of Medicine of The City University of New York, N. Y. 10029.

* Meglumine diatrizoate and sodium diatrizoate (Renografin-76, Squibb).

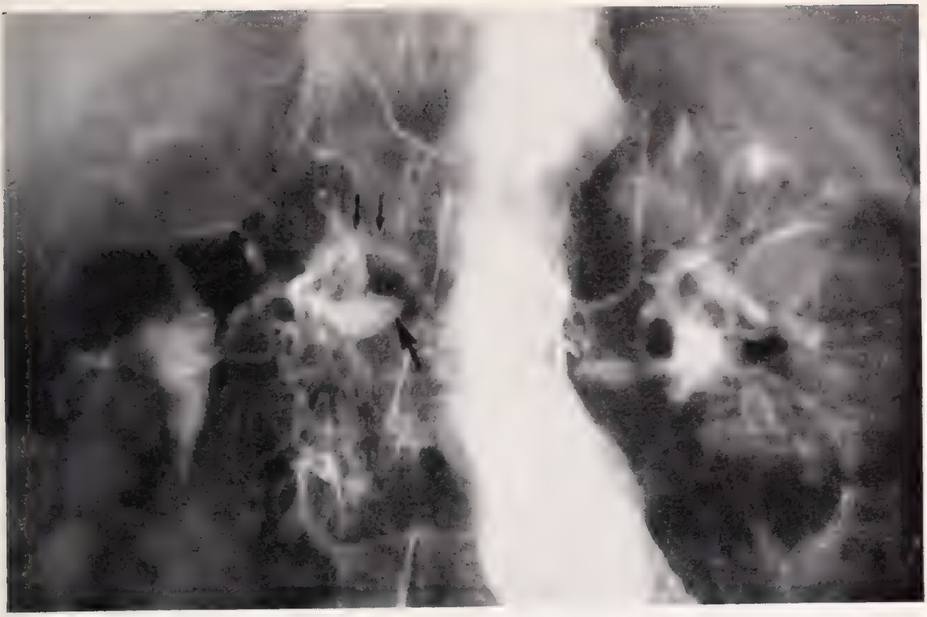
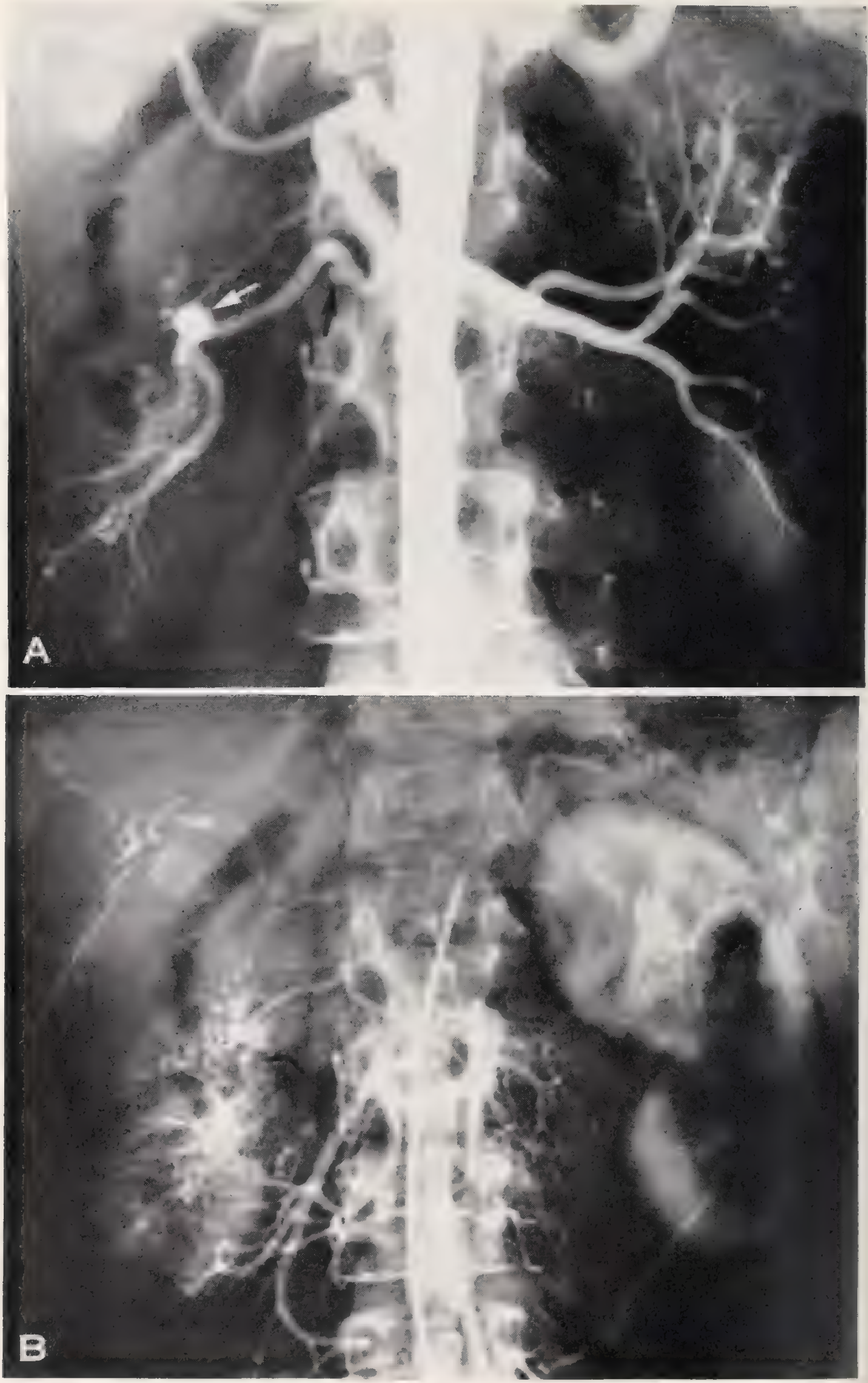


FIG. 1: Aortogram. The intrarenal arteries of the left kidney are well opacified. The post-stenotic segment of the right main renal artery (large arrow) is filled by collaterals from an enlarged lumbar artery (small arrows) by way of anastomosis with ureteral and capsular vessels. This tortuous route results in delayed opacification of the intrarenal branches.

Delayed opacification of the renal arteries may be seen in association with arteriosclerotic lesions as well as dysplastic lesions of the renal arteries (Fig. 1). Emboli often cause sufficient blockage of the renal arterial lumen to delay flow to the peripheral vascular bed. This process may also be associated with concomitant vasospasm, particularly in the acute phase. Aneurysms of the renal arteries result in delayed flow on the basis of obstructing thrombosis and/or eddying within the dilated segment (Fig. 2A, B). In addition, larger aneurysms may compress adjacent renal vessels so that flow in these vessels is also impaired (5). Compression secondary to encasement of renal arteries may occur in association with neoplasm, particularly carcinomas of the renal pelvis (6).

It should be emphasized that many stenotic lesions do not cause radiographically recognizable impairment of arterial flow and it may be difficult to assess the hemodynamic significance of an observed stenosis. It is in such patients that other parameters such as renal venous renin assay assume even greater importance.

Flow through the renal arteries can also be altered by the use of pharmacologic agents. Epinephrine in a dose of 5–10 micrograms is injected into the main renal artery as an aid in the diagnosis of renal carcinomas. Normal renal arteries constrict following epinephrine administration. Since tumor vessels do not respond in a normal fashion, these lesions become more obvious when epinephrine is administered just prior to the angiogram (13). This same vasoconstrictor effect can be used to improve renal venography. Normally, when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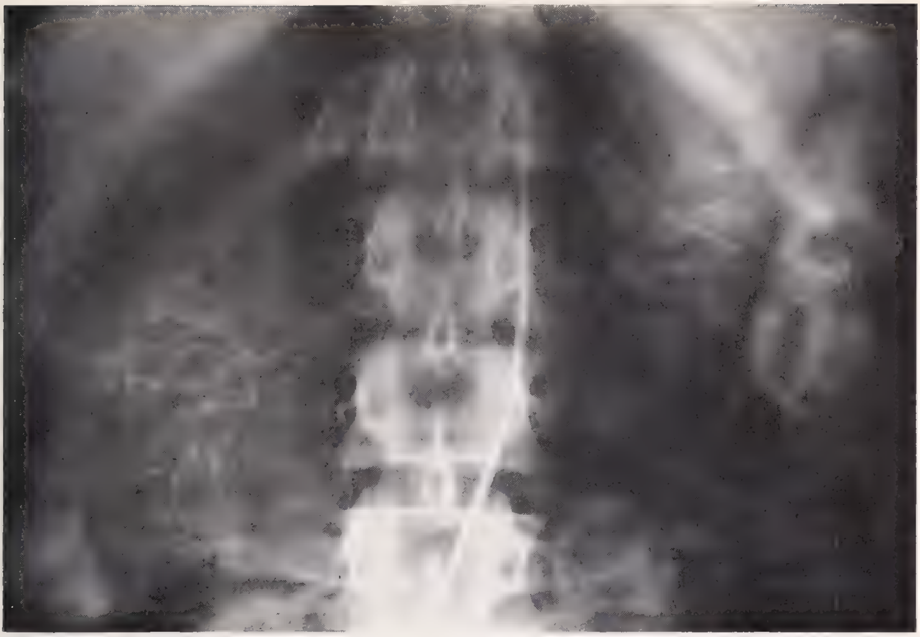

FIG. 3: Aortogram, delayed film in a patient with arteriolar nephrosclerosis. All of the aortic branches have emptied except the renal arteries. A nephrogram has not formed. This is a result of compromise of the runoff in these kidneys.

contrast material is introduced through a catheter directly into the main renal vein, only a few major tributaries are visualized because the rapid forward flow of blood in the vein washes out the contrast material. If epinephrine is first injected into the renal artery, the renal blood flow is so decreased that contrast material injected into the vein will easily reflux into smaller parenchymal veins.

Diffuse Parenchymal Processes

The renal parenchyma may be diffusely destroyed or the renal vascular bed may be widely altered, resulting in obliteration of small vessels. The increased resistance to runoff results in delayed washout of contrast material during aortography or selective renal angiography.

In evaluating patients in renal failure, one commonly sees prolonged opacification of the arterial system. These patients generally have advanced arteriolar nephrosclerosis or chronic glomerulonephritis although any diffuse parenchymal process can cause the same result if enough of the renal vascular bed is obliterated (Fig. 3), (7, 8).

Recently, the problem of evaluating transplanted kidneys has assumed considerable importance. The rejection phenomenon causes obliteration of smaller

FIG. 2: Aortogram of a patient with neurofibromatosis.
A: Early arterial phase. Several renal artery aneurysms are present on the right (arrows).
B: Late arterial phase. A normal capillary phase is seen in the left kidney. The intrarenal branches on the right remain opacified due to the impaired blood flow associated with the aneurysms.

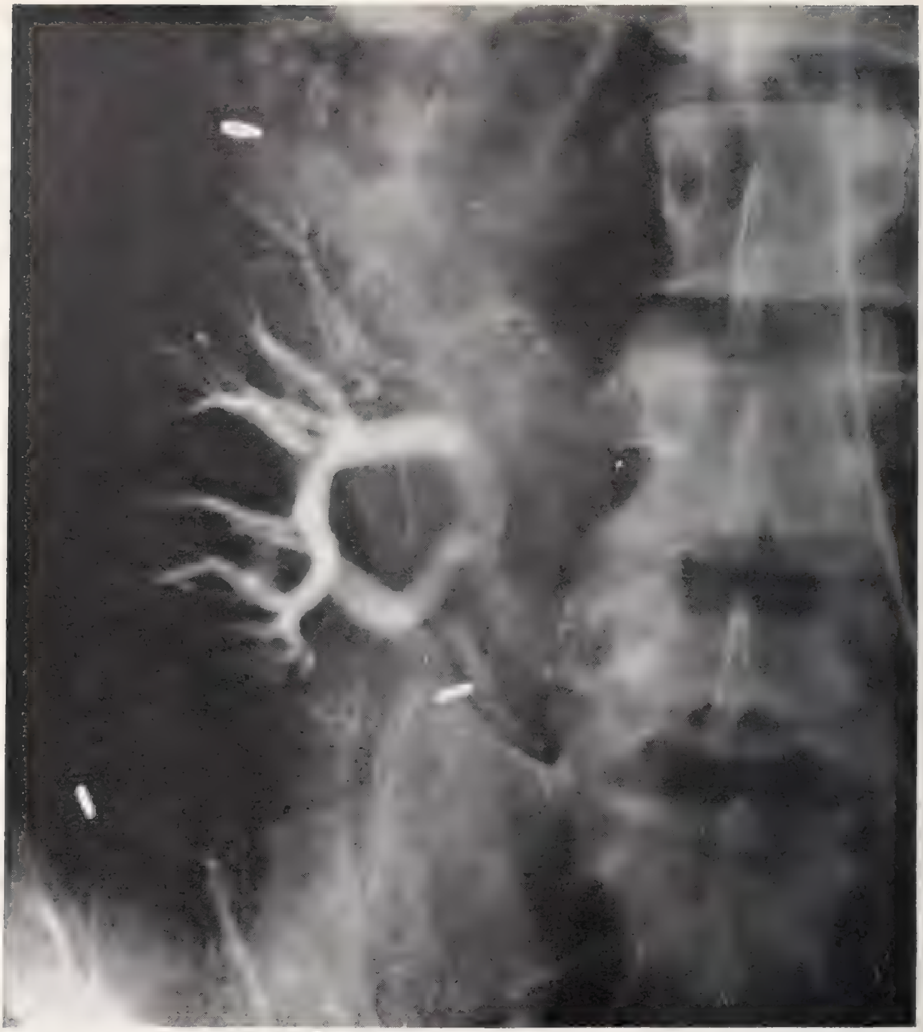

FIG. 4: Rejection of a transplanted kidney. Aortogram, late film. Rejection is associated with obliteration of small renal arteries and subintimal proliferation in larger branches. As a result there is delayed opacification of the major branches in this donor kidney while vessels of surrounding structures have emptied normally.

vessels as well as subintimal proliferation in larger vessels (9). Here again, the result is the destruction of the vascular bed of the kidney and so prolonged opacification of the major renal branches is observed (Fig. 4).

The peripheral vascular bed of the kidney may be compromised by pressure from masses extrinsic to the kidney. We have seen this occur with a perirenal hematoma. Such masses may cause sufficient renal ischemia to result in hypertension (10, 11, 12). For this reason, surgical intervention in the face of an otherwise benign process may be warranted if impaired arterial flow is demonstrated.

Renal Vein Obstruction

Thrombosis of the renal vein will result in delayed washout from the renal arteries (14). This is a direct result of impaired outflow from the kidney (Fig. 5A, B). In some cases, the thrombosis may be complicated by an underlying parenchymal process such as glomerulonephritis (15). Renal vein occlusion may also occur with neoplastic invasion of the vein (Fig. 6A, B). If adequate venous collateral flow is present proximal to the occlusion, arterial flow may return to

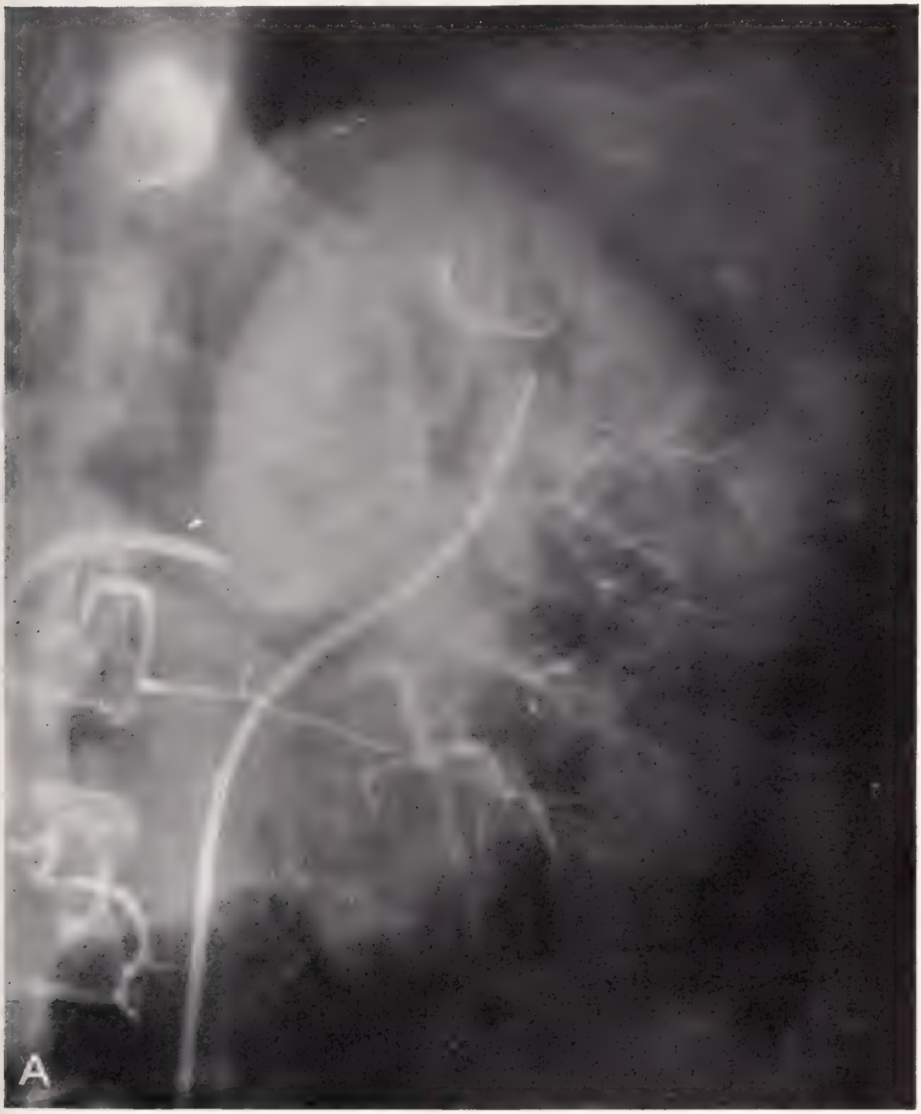

Fig. 5: Renal vein thrombosis.

A. Selective renal arteriogram. This film made at four seconds after the injection of contrast material reveals persistent opacification of the intrarenal arteries. Normally only a nephrogram should be seen at this time. A ureteral catheter is present in the renal pelvis.

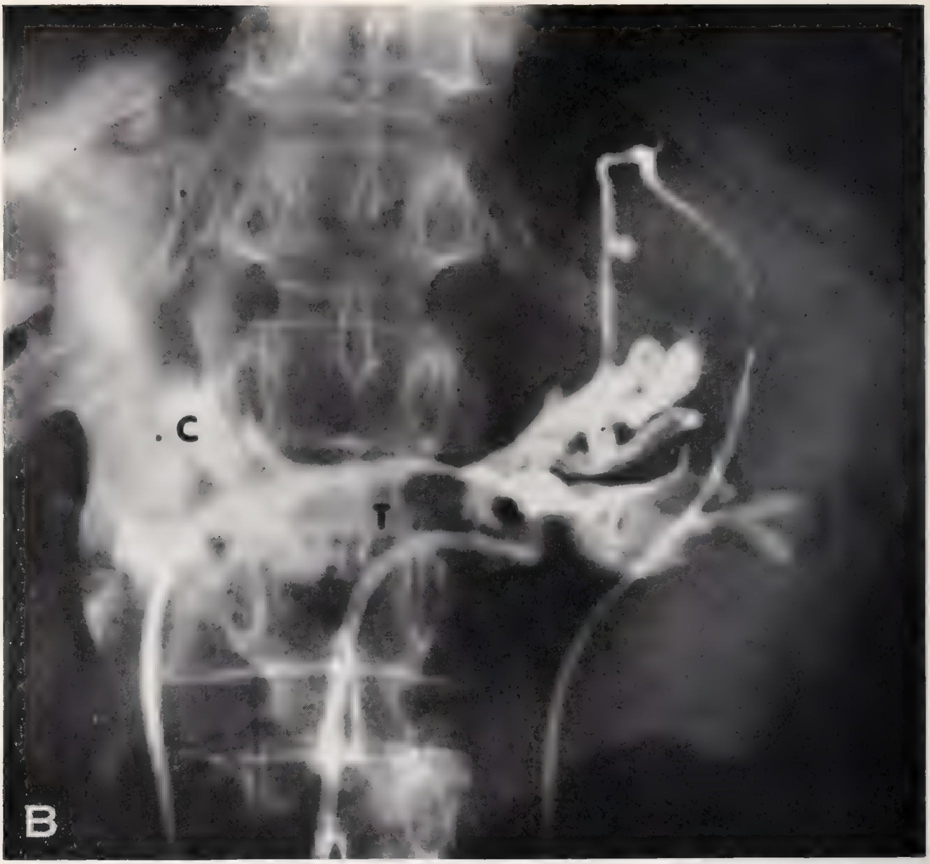

Fig. 5B.

B. Renal venogram. Contrast material has been injected into the renal vein demonstrating a lucent filling defect which proved to be a thrombus (T). This accounts for the poor emptying of the renal arteries seen in A. Some contrast material has refluxed into the inferior vena cava (C).

normal. This is particularly true of the left renal vein which has rich collateral paths via the gonadal, adrenal, and ascending lumbar veins.

Discussion

Serial filming at a known rate makes possible the assessment of abnormalities related to blood flow. An arterial stenosis that produces radiographic evidence of impairment of flow is more likely to be significant as a cause of hypertension. In those cases where a discrete arterial lesion cannot be demonstrated delayed arterial washout should indicate the need for cavography and renal venography to demonstrate a possible venous block. The presence of delayed washout of contrast material and a normal venous circulation usually means diffuse parenchymal disease compromising the runoff in the affected kidneys. This is most commonly seen in patients with the small kidneys of arteriolar nephrosclerosis or chronic glomerulonephritis.

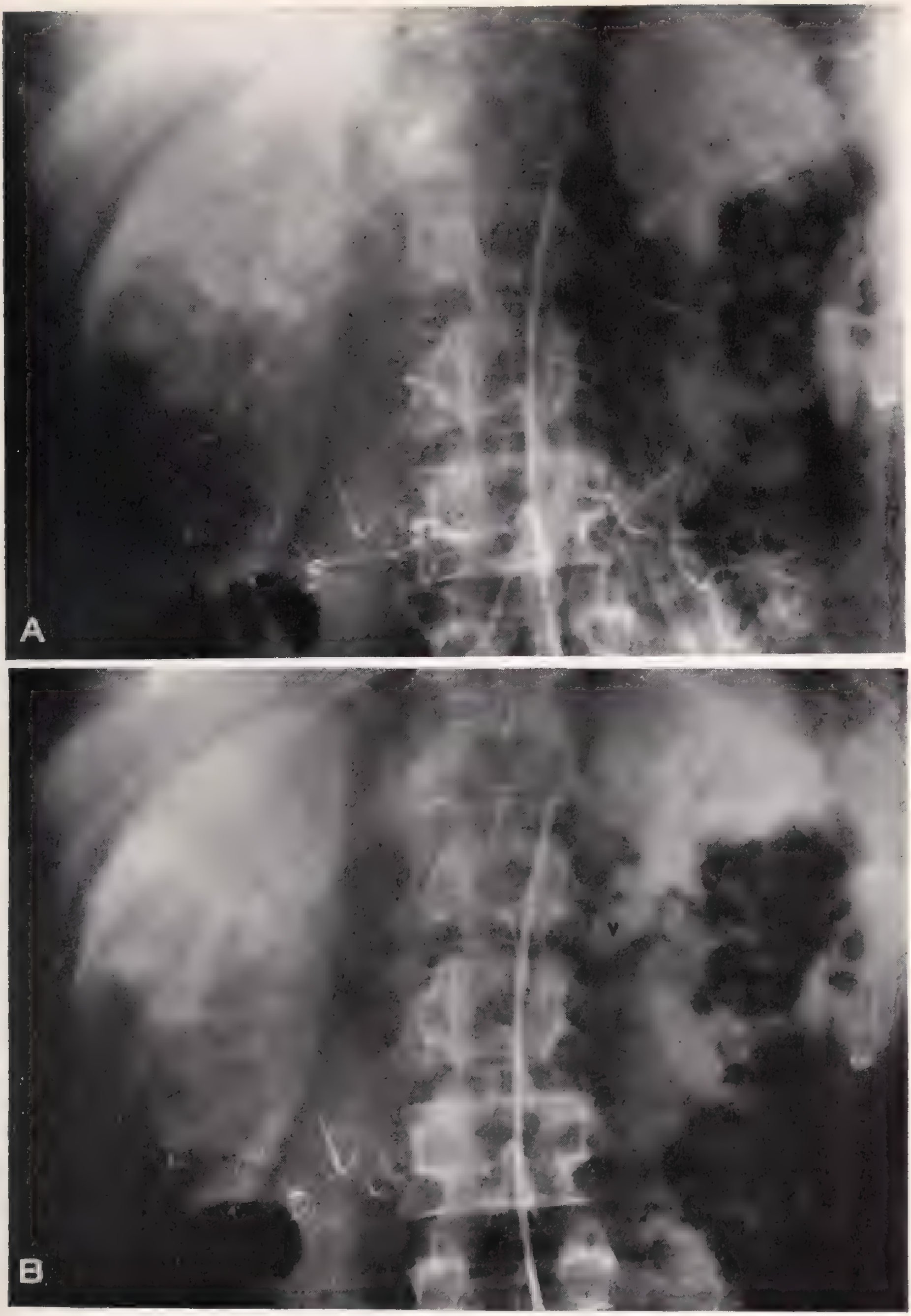

Fig. 6: Occlusion of the renal vein by a recurrent carcinoma of the colon.

A. Aortogram, late arterial phase. The normal left kidney demonstrates a nephrogram. The right renal arteries remain opacified.

B. Aortogram, venous phase. The normal left renal vein (V) is well opacified. The right renal vein is not seen as it has been occluded by tumor. The loss of a normal venous outflow accounts for the persistent arterial opacification seen in A.

The impairment of arterial flow associated with a stenosis may be further substantiated by studying renal venous washout time (16). This is done by opacifying the renal veins with 15 cc of contrast agent injected within ¾ of a second and recording the time necessary for the contrast material to be washed out. Normal renal venous washout time is 1.25 to 3 seconds. A washout time above 3 seconds is usually seen with a significant arterial stenosis or diffuse parenchymal disease.

The radioisotopic renogram and the arteriogram are often complimentary procedures. Arteriography has the advantage of demonstrating the location and extent of an arterial lesion. In addition, intrarenal segmental branch stenoses which may be responsible for hypertension are demonstrated by arteriography, but are often not detected by radioisotopic renography.

Analysis of technique is important in the evaluation of radiographic findings during angiography. Catheter size and placement, number and location of catheter side holes, injection rate and volume, and filming rate should be standardized to make patient comparisons more feasible. Certain pitfalls in assessing these studies must be kept in mind. For example, since 20 percent of the patients have two renal vessels supplying a kidney, the placement of the catheter at a level between two vessels during aortography may give the false impression of slow flow in the lower part of the kidney. This results from the transient perfusion of the upper vessel by reflux while the lower vessel is perfused longer and later. Similarly, during selective renal angiography, the catheter tip may be passed beyond a branch so that the corresponding segment of the kidney will be perfused only by reflux which occurs later and for a shorter period of time.

Summary

Late or prolonged opacification of the renal arteries in the absence of technical or iatrogenic cause is usually indicative of pathology. Often the underlying cause is apparent from the intravenous urogram or angiogram. The presence of altered arterial flow is confirmatory evidence of the functional significance of the anatomic lesion. In those cases where an obvious cause is not apparent, further appropriate evaluation is indicated.

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Gastrocolic Fistula Secondary to a Benign Gastric Ulcer: A Case Report and a Review of the Literature

M. Haimov, M.D., G. Garami, M.D., and A. Belman, M.D.

Gastrocolic fistula complicating the course of a benign gastric ulcer is a rare occurrence. The Mayo clinic has reported seeing only one case of this type in their entire experience (1). We have recently treated a 49-year-old female with a gastrocolic fistula caused by a benign gastric ulcer. This patient will be the subject of this report.

Case Report

A 49-year-old Caucasian woman was admitted to the Elmhurst General Hospital with a chief complaint of epigastric pain, diarrhea, and malodorous vomiting associated with a 30-lb weight loss.

Her abdominal symptoms started about seven years prior to this admission. At this time she began complaining of epigastric pain relieved by food, milk, and antacids. A duodenal ulcer was diagnosed and she responded well to medical management. Two years later she was hospitalized with upper gastrointestinal bleeding which again responded to conservative treatment.

Six weeks prior to admission the patient developed epigastric pain which this time was only partially relieved by diet and antacids. She had repeated episodes of vomiting, frequently feculent in nature and malodorous. Each meal was followed by explosive diarrhea which contained undigested food. The patient became very weak and lost 30 lbs of weight. There was no history of ingestion of any steroid medications.

Physical examination on admission revealed a malnourished, white female appearing dehydrated and chronically ill. The abdomen was soft with epigastric tenderness and fullness suggestive of a mass in this region. The lower extremities were markedly edematous. The pertinent laboratory findings were: hemoglobin 9 mg%; albumin, 1.9 mg%, and a stool positive for occult blood.

X-ray findings: Upper GI series demonstrated a gastric ulcer connected through a fistulous tract with the transverse colon. The sequence of filling of the involved structures is demonstrated in Fig. 1. The stomach is seen filled with barium with greatly thickened folds radiating towards the greater curvature aspect of the antrum. From there, the barium is seen passing through a gastric defect and through a fistulous tract into the transverse colon. The colon can be identified by the haustral pattern in this view. In the later films there was filling of the remainder of the transverse colon. The lack of nodularity or irregularity in the stomach, fistula, or colon made a neoplastic process improbable. In the absence of previous surgical or traumatic history, benign inflammatory processes such as diverticulitis, granulomatous disease or gastric ulcer were considered, with the latter diagnosis the most likely because of the smooth-surfaced gastric folds radiating in stellate fashion toward the greater curvature perforation.

Hospital course: After intensive preoperative preparation, the patient was operated upon. An inflammatory mass involving the greater curvature of the stomach and the midtransverse colon was found. This mass was caused by the large gastric ulcer which had perforated into the colon. A partial gastrectomy, Billroth II-type, and transverse colon resections were performed. The proximal end of the colon was exteriorized as an end colostomy and the distal end was brought out through a separate incision as a mucous fistula.

From the Department of Surgery and the Department of Radiology, The Mount Sinai Hospital Services, City Hospital Center at Elmhurst; and Mount Sinai School of Medicine of The City University of New York, N.Y. 10029.

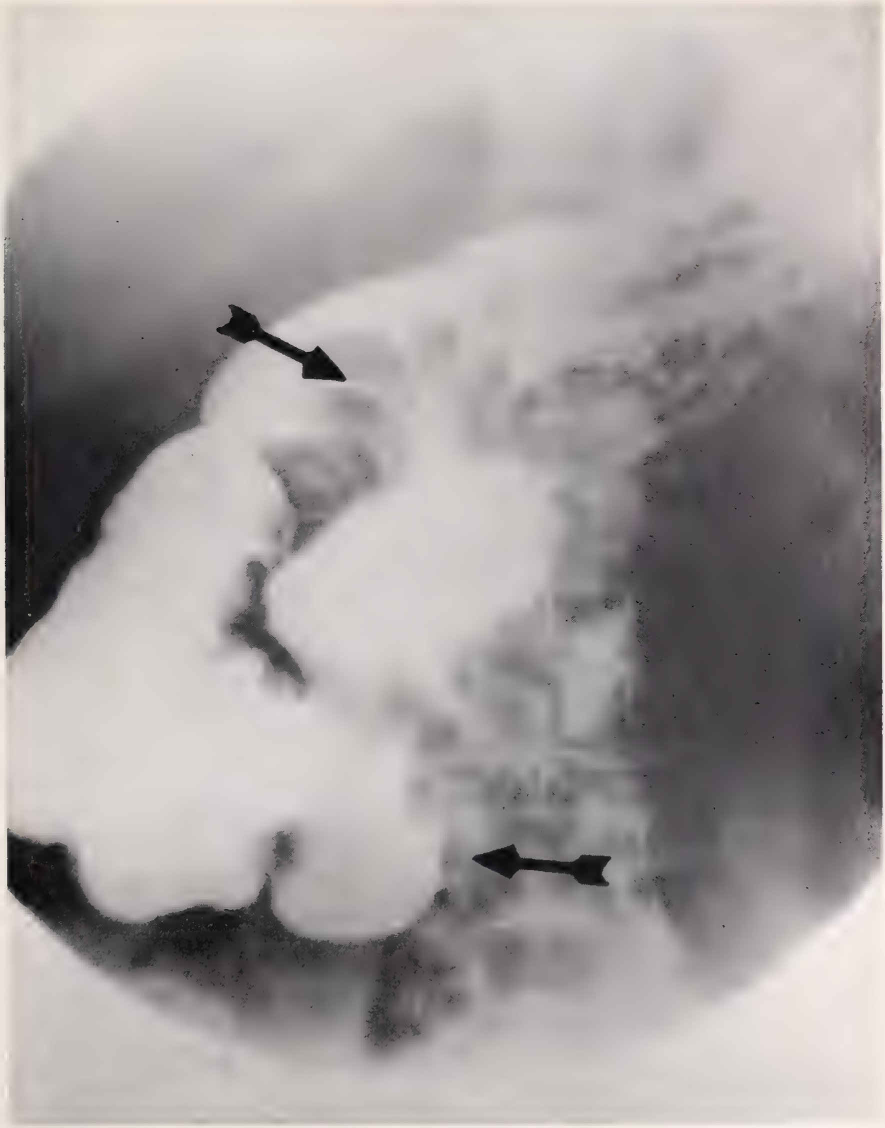

FIG. 1: Spot film demonstrating the passage of barium from the stomach ulcer (arrow) through a fistulous tract into the colon (two arrows).

Pathologic examination of the excised specimen revealed a deep penetrating gastric ulcer which extended to the serosa of the large intestine (Fig. 2). The ulcer measured 3 × 3 × 2 cm. The bed of the ulcer was firm, rough and focally hemorrhagic. It extended into the large intestine through a fistula measuring 1 × 1 cm. Microscopic examination showed a deep penetrating gastric ulcer covered with fibrinous exudate containing fragmented leukocytes. The underlying muscular layer was markedly hypertrophied and showed granulated tissue containing lymphocytes, plasma cells and an occasional eosinophil. There were numerous hypertrophied nerve bundles and sclerosed vascular channels with organized thrombi.

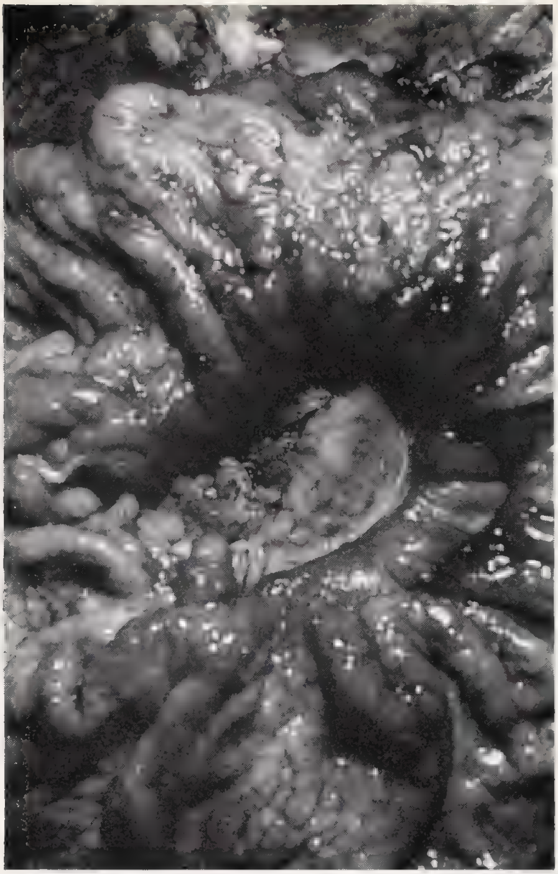

FIG. 2: Close-up of the gastric ulcer. The fistulous tract and colonic mucosa are visible in the base of the ulcer.

Sections from the fistula showed continuity of the antral and colonic mucosa. The sections from the fundus showed remarkably increased numbers of parietal cells.

The postoperative course was uneventful. The patient was discharged and followed in the Outpatient Department. She became asymptomatic and her nutritional status markedly improved. Four months after the initial surgery she was readmitted and the colon continuity was reestablished with a right-to-left colon anastomosis. Her postoperative course was again uneventful and she has remained well since.

Discussion

Most of the gastrocolic fistulae seen in clinical practice are those resulting primarily from perforations through carcinomas of the colon or stomach (2). In a series of 507 consecutive carcinomas of the stomach, Dickson (3) reported a 2% incidence of fistula formation. Marshall et al (4) found that 0.5% of 5400 cases with gastric and colonic carcinoma developed complications. In the majority of cases, the primary reason is a far advanced colon neoplasm. Carcinoid tumors of the colon (5), chronic ulcerative colitis (6) and trauma are other rare causes of gastrocolic fistulae. Five of the reported cases of benign gastric ulcer penetrating into the colon have been in patients taking steroid medications (7, 8, 9, 10, 11). In this group of patients, an ulcer in the antrum along the greater curvature is known to occur. This is an ideal anatomic position for a penetrating ulcer to develop into a gastrocolic fistula, taking into account the minimal inflammatory reaction around an ulcer bed characteristic to ulcers related to steroid therapy. One neonatal gastrocolic fistula has been reported (12) leaving nine reported cases associated with the common variety of benign gastric ulcer (14, 15, 16, 17, 18, 19, 20, 21).

The clinical picture is fairly characteristic: feculent vomiting in the absence of intestinal obstruction; diarrhea containing undigested food; weight loss and malnutrition. The diagnosis can be confirmed with an upper gastrointestinal series as in this case, or as pointed out in the literature, more frequently with a barium enema. Surgery is the treatment of choice, but only after careful preoperative preparation which should include correction of anemia, electrolyte imbalance, vitamin deficiency and hypoproteinemia. This preparation is vital in order to avoid the prohibitive mortality which accompanies operating on these patients without adequate preoperative preparation, which should include mechanical cleansing of the large intestine. The decision to use a one- or two-stage procedure would have to be made on the operating table.

Summary

A case of gastrocolic fistula resulting from a benign gastric ulcer is reported. The pertinent literature concerning the frequency of this complication, its symptomatology and management has been reviewed.

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RADIOLOGIC NOTES

CLAUDE BLOCH, M.D. AND HARVEY M. PECK, M.D., COEDITORS

CALCIFICATIONS IN GASTROINTESTINAL MALIGNANCY—AN IMPORTANT CLUE IN RADIOLOGIC DIAGNOSIS

Submitted by
Jerome A. Gold M.D.

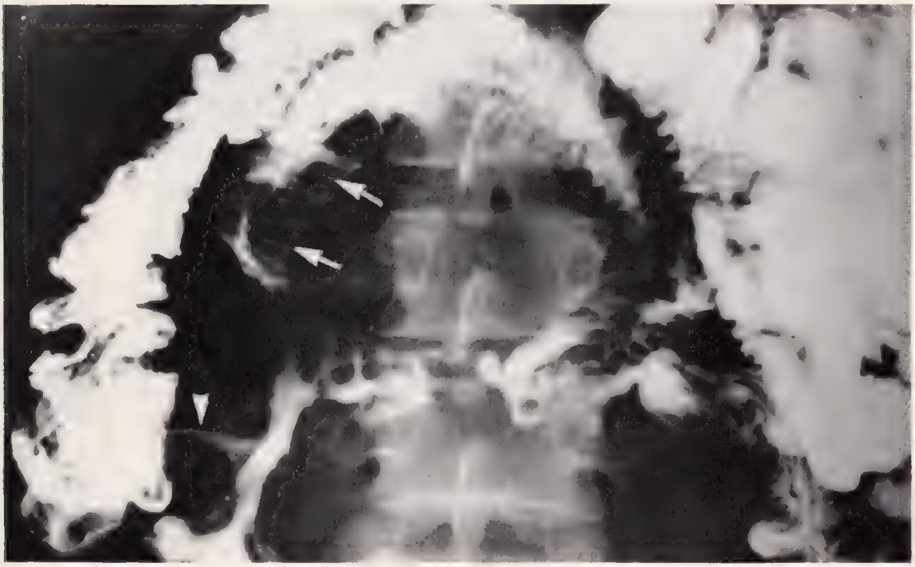
CASE NO. 347

This 30-year-old woman was admitted with the chief complaint of abdominal pain, abdominal mass, and anemia. A small bowel examination performed in May 1968 revealed narrowing of the terminal ileum which was suggestive of ileitis. (Fig. 1) She was treated with Sulfathalidine with only fair results. She was admitted to the hospital because of an iron deficiency anemia, abdominal pain, and an enlarging abdominal mass.

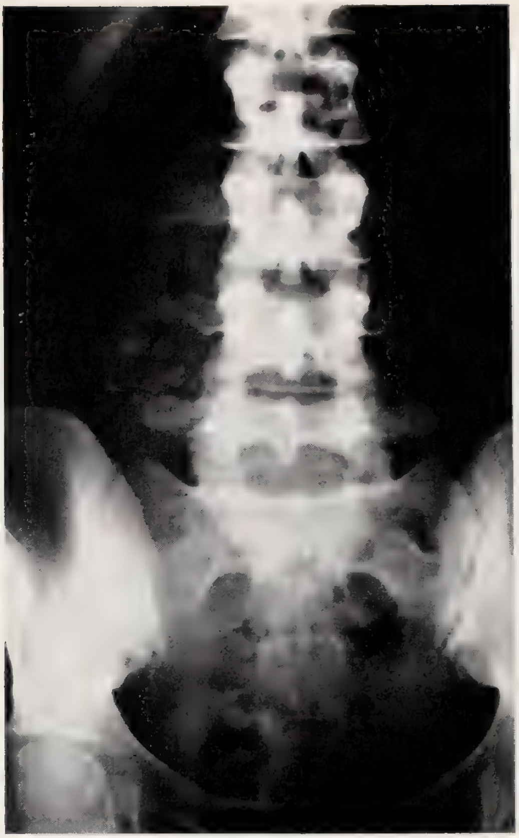
History and review of systems were noncontributory.

Upon admission to the hospital her vital signs were normal. Physical examination revealed pale conjunctiva and a large lower abdominal mass.

Laboratory evaluation revealed: ESR, 48; Hgb, 9.6; and WBC, 5,400. Barium enema showed a large mass within the right lower quadrant. A globular mass



Case 347, Fig. 1. Small bowel examination reveals narrowing, nodularity, and ulceration of the terminal ileum (short arrow). There is no evidence of obstruction. The remaining small bowel is normal in appearance. The calcifications are obscured by overlying barium (long arrows).



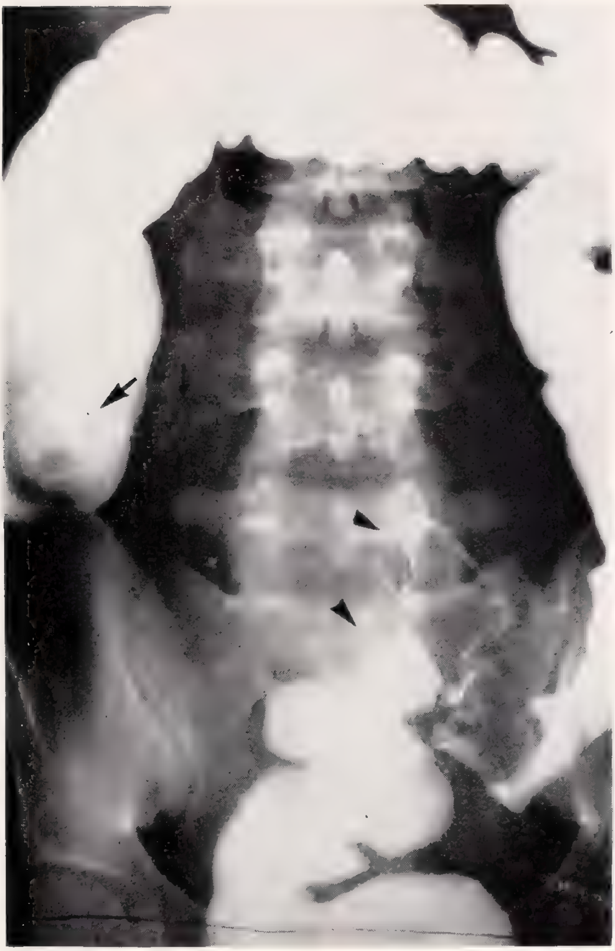
Case 347, Fig. 2. PA film of the abdomen demonstrates mottled, granular calcifications in the right lower quadrant varying from 1–3 mm in size (between arrows).

within the cecum suggested either a mass arising from the ileocecal valve or intussusception of a mass into the cecum. Calcific densities were noted in the right lower quadrant. (Fig. 2) A pelvic mass angulated and fixed the sigmoid colon with possible infiltration of the bowel wall. (Fig. 3) These findings were thought to be compatible with a diagnosis of ileitis and abscess, tuberculosis, or a tubo-ovarian abscess.

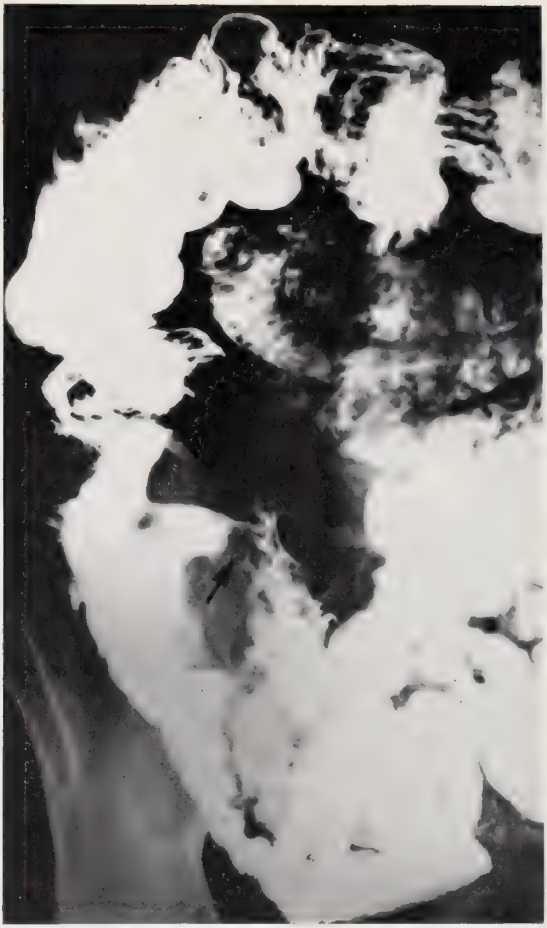
An upper GI series and small bowel examination revealed several loops of ulcerated small bowel in the distal ileum. The terminal ileum was stenotic and severely ulcerated. (Fig. 4) These findings suggested the following diagnoses: regional enteritis, tuberculosis, or lymphosarcoma. The calcifications were thought to represent either enteroliths or tuberculous adenopathy.

Gynecologic evaluation suggested pelvic neoplasm. Sigmoidoscopy was normal.

Surgical exploration revealed generalized abdominal carcinomatosis from a primary mucin-secreting tumor of the ileocecal valve. A biopsy of the pelvic mass revealed ovaries infiltrated by mucin secreting adenocarcinoma.



Case 347, Fig. 3. Barium enema demonstrates a globular filling defect in the cecum (large black arrow) with adjacent calcifications (between small black arrows). The sigmoid colon is fixed, angulated, and infiltrated by a mass in the pelvis (short arrow).



Case 347, Fig. 4. Repeat small bowel examination reveals progressive ulceration and narrowing of the terminal ileum (arrow). A loop of ileum is draped around a mass. Calcifications are faintly seen adjacent to the terminal ileum.

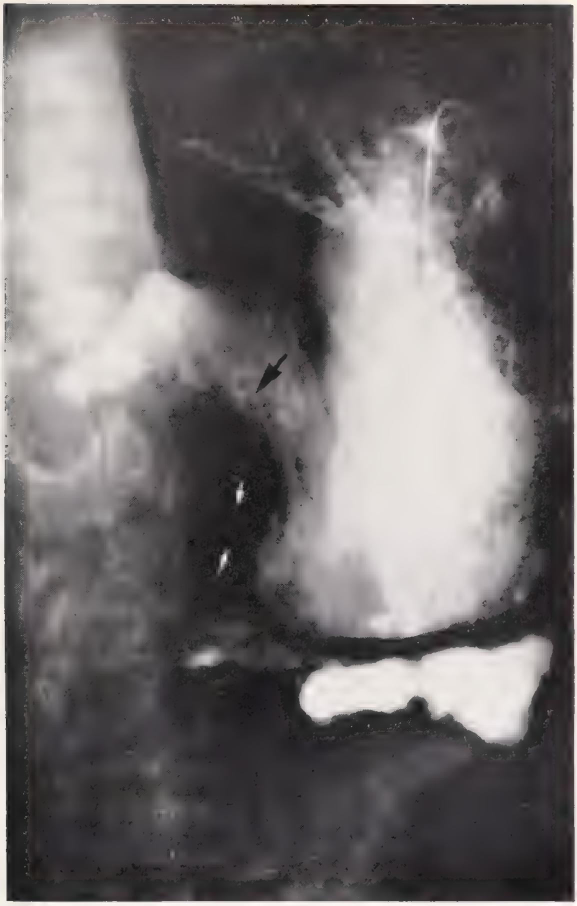
Postoperatively, the patient was started on a course of 5-Flurouracil which was continued on an outpatient basis.

CASE NO. 348

A 68-year-old woman was admitted to the hospital because of vomiting. A carcinoma of the transverse colon had been removed three years prior to admission.

Physical examination revealed a mass in the epigastrium and an enlarged liver.

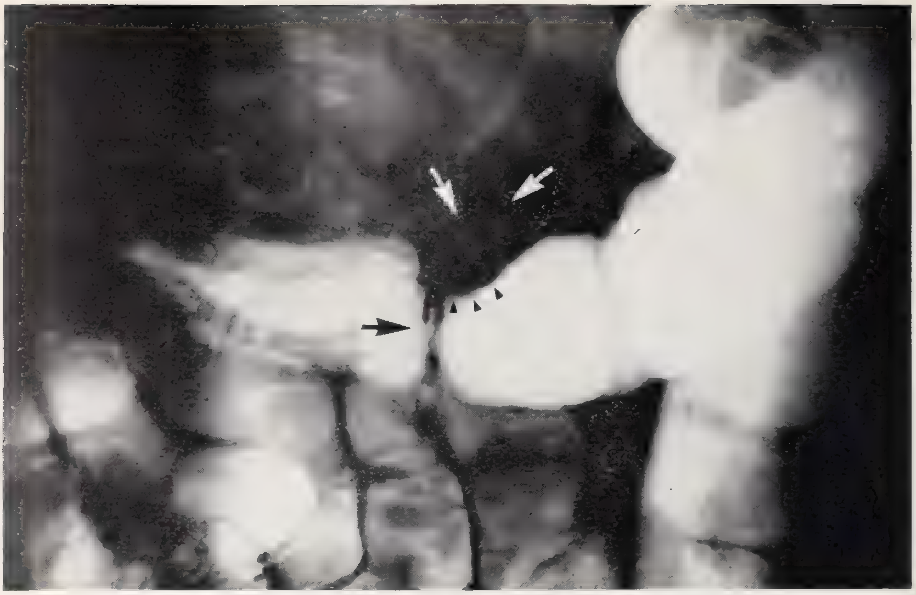
Laboratory evaluation disclosed an iron deficiency anemia, electrolyte disturbances consistent with protracted vomiting, and an elevated alkaline phosphatase.



Case 348, Fig. 1. An upper GI series reveals retained secretions in the stomach indicative of gastric outlet obstruction. The antrum is elevated and narrowed by an extrinsic mass (black arrow). Small calcifications are faintly seen in the region of the mass (between white arrows).

An upper GI series revealed an excessive amount of retained secretions in the stomach indicative of gastric outlet obstruction. The gastric antrum was narrowed and elevated by a mass compressing the greater curvature. Small granular calcifications were faintly seen in the region of the mass. (Fig. 1)

A barium enema demonstrated the site of previous resection in the transverse colon. The colonic mucosa in this area was intact and there was no evidence of obstruction. (Fig. 2) The superior aspect of the colon at the site of the previous resection was slightly flattened by an extrinsic mass. A group of small, punctate calcifications was also seen in this region corresponding to those seen along the greater curvature of the gastric antrum. (Fig. 2)



Case 348, Fig. 2. Barium enema demonstrates the site of previous resection in the transverse colon (black arrow). The superior aspect of the colon just distal to the anastomosis is indented by an extrinsic mass (black arrowheads). A group of clumped, punctate calcifications (white arrows) is seen in the region of the extrinsic mass.

Exploratory laparotomy confirmed the presence of metastatic mucin-producing carcinoma obstructing the gastric antrum. A palliative gastroenterostomy was performed.

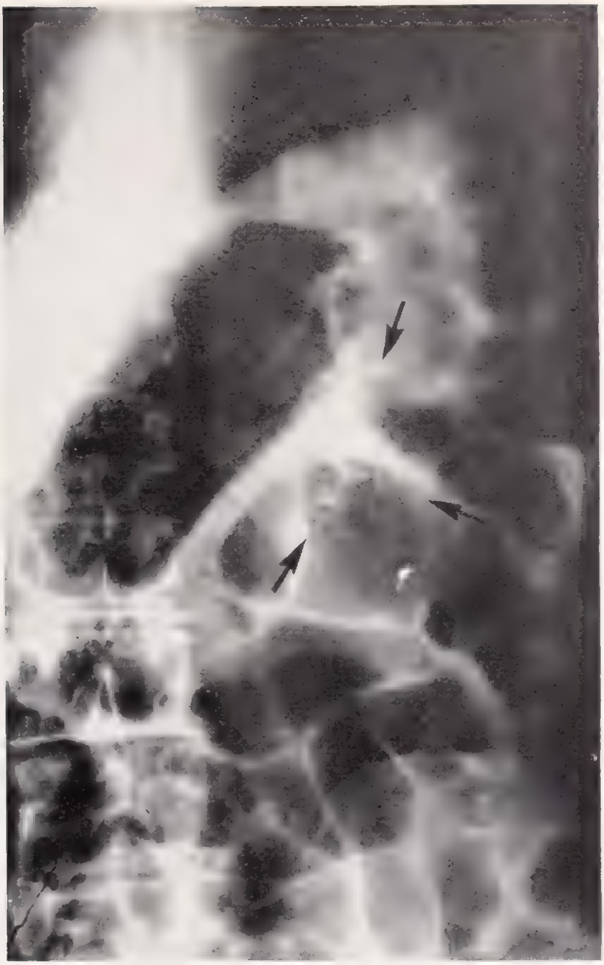
CASE NO. 349

This 69-year-old male was in good health until he began to experience epigastric pain unrelated to meals. There was no history of hematemesis or gross melena. He had lost about 10 lbs in weight.

Physical examination revealed a palpable liver. Laboratory examination revealed anemia and an elevated alkaline phosphatase.

A plain film of the abdomen revealed a hazy density on the left upper quadrant composed of aggregates of punctate calcifications. (Fig. 1) An upper GI series revealed a typical scirrhous carcinoma of the stomach with calcifications present in the thickened gastric wall.

At laparotomy an unresectable mucin-producing gastric carcinoma was found with regional and hepatic metastases.

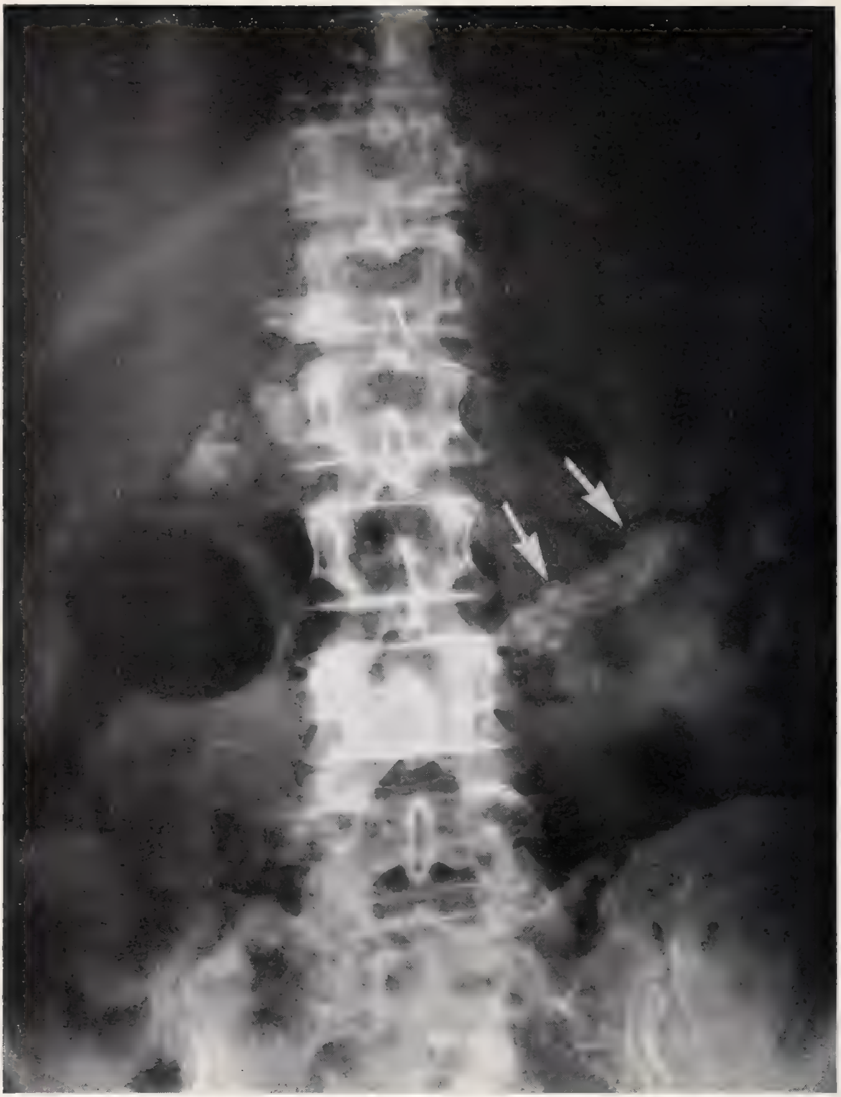


Case 349, Fig. 1. Plain film of the abdomen reveals a hazy density in the left upper quadrant composed of aggregates of punctate calcifications (black arrows). A subsequent upper GI series confirmed the presence of an ulcerating scirrhous carcinoma of the stomach with calcifications in the infiltrated gastric wall.

CASE NO. 350

This 65-year-old woman was admitted to the hospital because of epigastric pain and weight loss. There was no history of vomiting or melena. Physical examination revealed a pale, elderly female with a pelvic mass. Laboratory evaluation disclosed anemia.

Preliminary film of the abdomen demonstrated ill-defined, coarse, clumped calcifications along the transverse colon. (Fig. 1.) Other similar intraabdominal



Case 350, Fig. 1. Plain film of the abdomen demonstrates ill defined, coarse, clumped calcifications along the transverse colon (white arrows). Such a long segment of calcification should suggest calcified metastases rather than a calcified primary carcinoma of the colon.

calcifications were also noted. Increased density in the pelvis suggested a pelvic mass.

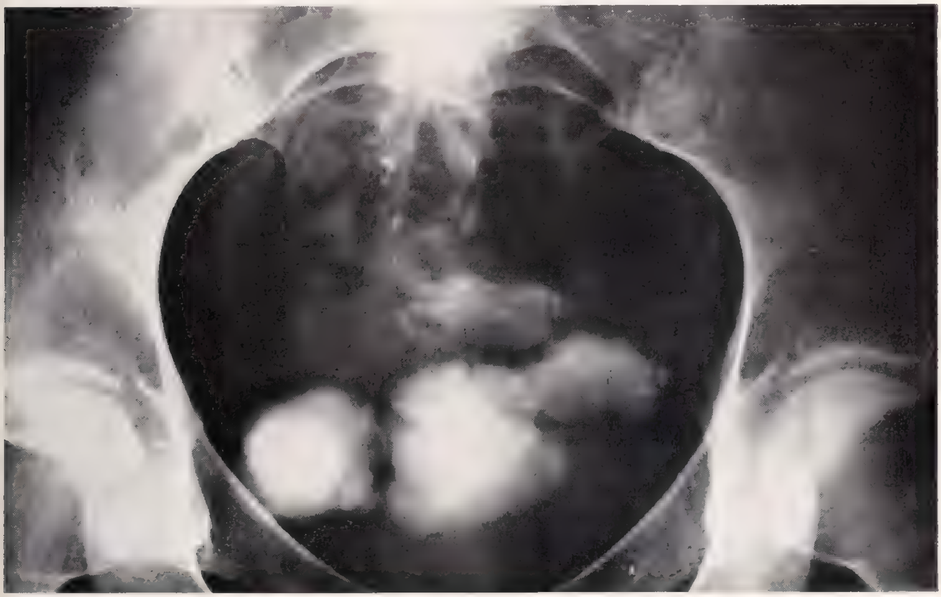
A laparotomy and biopsy disclosed a papillary mucinous adenocarcinoma of the ovary with peritoneal metastases. Implants were noted along the transverse colon and transverse mesocolon.

CASE NO. 351

This 33-year-old woman sought medical attention because of persistent crampy abdominal pain. There was no history of diarrhea or melena.

Physical examination revealed a pelvic mass.

A plain film of the abdomen revealed amorphous, heavily calcified masses within the pelvis. (Fig. 1) The configuration of the calcifications suggested the possibility of a calcified colonic neoplasm. A barium enema examination revealed that the colon was intrinsically normal.



Case 351, Fig. 1. Plain film of the abdomen reveals amorphous, heavily calcified masses within the pelvis. A barium enema demonstrated that the sigmoid colon was intrinsically normal. The histologic diagnosis was bilateral calcified mucinous adenocarcinoma of the ovary.

The histologic diagnosis after laparotomy and biopsy was bilateral, calcified mucinous adenocarcinoma of the ovary.

Discussion of Cases 347–351

Psammoma bodies are calcified, nonbirefringent, laminated concretions which measure 5 to 100 microns in diameter. They are seen by the pathologist most commonly in tumors of the ovary, thyroid, breast, and in meningiomas. Similar calcifications are identified histologically with far less frequency in mucin-producing tumors of the gastrointestinal tract. Their formation is due to a combination of the physico-chemical properties of the glyco-proteins within mucin and local pH changes within the tumor (1, 2, 3). The histologic presence of these calcifications is rarely correlated with their radiographic identification because of their small size. It is only when the mass of tumor tissue is sufficiently large and the concentration of calcifications within the mass is sufficiently high, that they may be seen on an abdominal roentgenogram.

Lingley (4) described granular, sand-like calcifications (psammoma bodies) in papillary tumors of the ovary. These calcifications may be seen in benign or malignant tumors of the ovary. They may also appear as diffuse calcification of the abdominal mesentery when metastatic ovarian carcinoma becomes widespread throughout the abdomen. Metastatic calcifications along the wall of the gastrointestinal tract are usually coarser and more diffuse than those calcifications seen in primary carcinomas of the stomach or colon. (Case No. 350) Psammomatous calcifications may also be seen within the ovaries when there is metastatic disease to the ovaries from primary mucin-producing tumors of the gastrointestinal tract (Kruckenberg Tumor). Occasionally, very dense ovarian calcifications may be confused with a calcified carcinoma of the sigmoid colon. Such dense calcification of a large mass is usually not seen in primary carcinoma of the GI tract, although a barium enema should be performed to exclude this possibility (Case No. 351).

The appearance of psammoma-like calcifications within the wall of the gastrointestinal tract, although extremely unusual, should strongly suggest the diagnosis of a mucin-producing carcinoma. There are approximately fifteen cases of calcifications within gastric carcinoma reported in the literature (1, 2, 5, 6, 7). These calcifications usually outline the wall of the stomach and have the classical appearance of psammomatous calcifications. The gastric wall is usually thickened and there is evidence of mucosal destruction, ulceration, or mass on barium contrast studies. The uniform distribution of these calcifications suggests that tissue necrosis does not play a significant role in their formation but rather that it is the specific properties of the mucin within the tumor.

Calcifications within a carcinoma of the stomach can usually be distinguished from other causes of gastric calcification. The calcifications within gastric leiomyomas are localized and have the flaky appearance of calcifications commonly observed within uterine fibroids (8). Calcification of the wall of the stomach also occurs in hypoparathyroidism, vitamin D intoxication, and as the result of chemical necrosis, particularly calcium chloride used in the treatment of neonatal tetany (9). These calcifications may occasionally resemble psammoma bodies but other evidence of neoplasm will be lacking.

Twelve cases of calcified carcinoma of the colon have been reported up to the present (10, 11, 12, 13, 14, 2, 15, 3, 16). Most of these cases exhibited typical psammomatous calcifications although at least two cases have been reported where the calcifications were coarse or dumbbell-shaped (16, 17). Ossification has also been reported in colonic carcinoma (11). These non-psammomatous calcifications are probably the result of tumor necrosis rather than the physico-chemical properties of mucin. Occasionally, calcification within the wall of the colon may be mistaken for a thin coating of barium.

Calcified colonic carcinoma as well as calcified gastric carcinoma appear to have a predilection for younger patients. Shockman (18) has reported a case of a 46-year-old male with chronic ulcerative colitis who developed a calcified colonic carcinoma. The appearance of calcification within a stricture (19, 20, 21) or within the colonic wall of a patient with chronic ulcerative colitis may therefore be further evidence of malignant degeneration.

Several conditions involving the right lower quadrant may have associated calcifications which can be differentiated from those arising in a mucous producing tumor of the colon. These include: pericecal abscess; mucocele of the appendix; myxoglobulosis; calcified congenital duplications, and enteroliths. The calcifications of pericecal abscess, mucocele or myxoglobulosis are usually larger, coarser, or more discrete (22). Enteroliths, calcified concretions within the bowel which are thought to form because of chronic obstruction or stasis, are larger or have lamellations. Active tuberculous enteritis is frequently not associated with calcified mesenteric adenopathy (23). Calcified caseous nodes are readily distinguished from psammomatous calcifications.

Case Reports: CALCIFICATIONS IN GASTROINTESTINAL MALIGNANCIES

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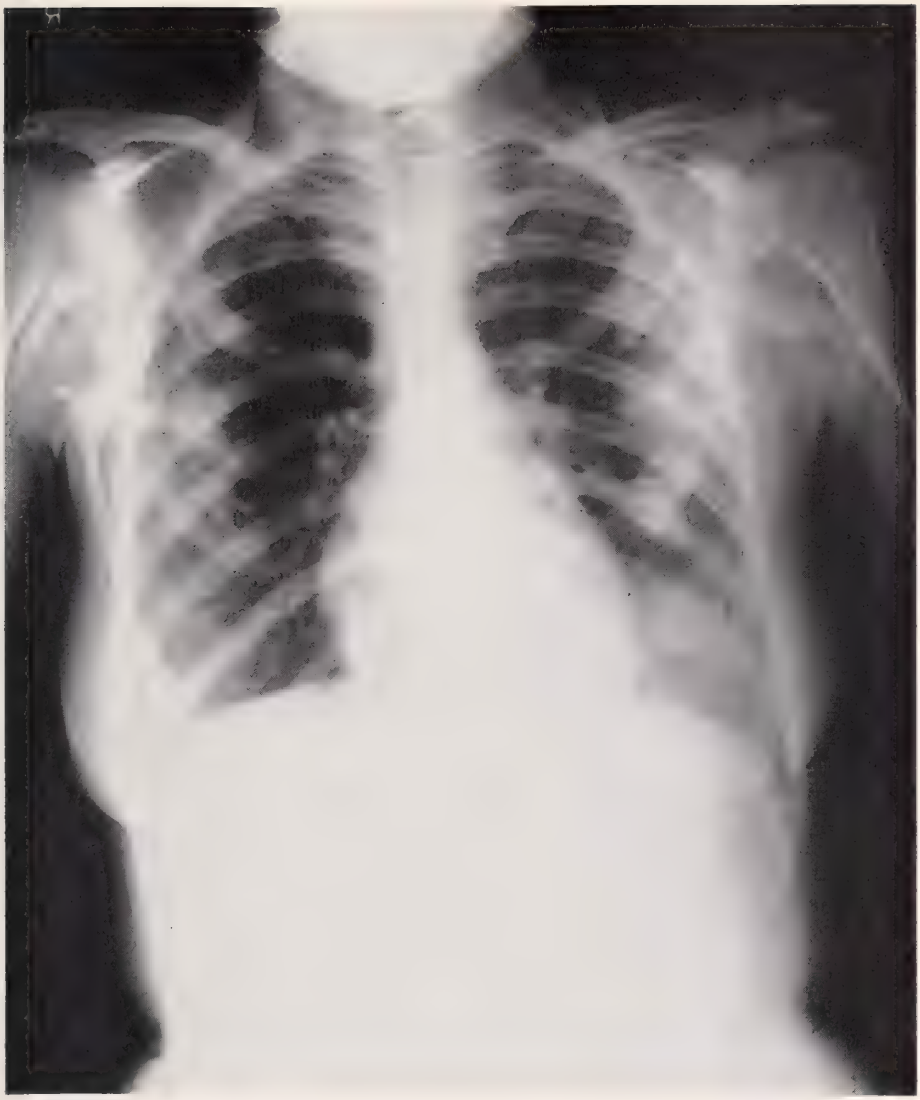
Myositis Ossificans Progressiva

Submitted by
Alan J. Simpson, M.D. and Stanley Friedman, M.D.

CASE NO. 352

This 19-year-old female was first admitted to the obstetric service because of an incomplete septic abortion. She also complained of limitation of motion of the neck and shoulder. The patient was born with deformed digits of both hands. Two years prior to admission, the patient first noted limitation of neck and shoulder motion, which was associated with red hot swollen areas over the sternocleidomastoid and pectoralis muscles. The swellings lasted one month and disappeared, only to be replaced by progressive bony masses. One year prior to admission, the patient sustained trauma to the left jaw. This was followed by hardening of the left cheek and gradual inability to open the jaw. The patient also noted progressive hardening of the muscles in the paraspinal region and latissimus dorsi. The family history was noncontributory. Physical examination revealed a palpable hard mass in the left neck, hardened paraspinal, pectoralis, latissimus dorsi, and trapezius muscles, and scoliosis of the thoracic spine. A bilateral hallux valgus and a shortened, deformed little finger of both hands were also noted. Laboratory data revealed a normal alkaline phosphatase, calcium, phosphorus, creatinine, and lupus erythematosus prep. Eosinophil count was 2%; however, the patient had positive stools for hookworm and schistosoma.

Roentgen studies disclosed extensive ossification involving the soft tissues and musculature of the chest, back, and abdomen (Fig. 1A, 1B, and 2). The areas of bone formation were sharply demarcated and tended to assume orientation along the axis of the pectoralis, latissimus dorsi, trapezius, psoas, and paraspinal muscles. Exostoses of both upper tibia and the distal left femur were noted in the region of probable tendon insertions. Radiographs of the feet (Fig. 3) revealed a bilateral hallux valgus deformity. The distal phalanges of the first, third, fourth, and fifth toe were fused bilaterally. The first metacarpal was shortened bilaterally and a hypoplastic middle phalanx of the second toe was



Case 352, Fig. 1A. PA view of the chest reveals extensive ossification along the muscle planes of the pectoralis, latissimus dorsi, and trapezius muscles. These are sharply demarcated and tend to assume linear oblique configuration.

present. A radiograph of the hands (Fig. 4) demonstrated bilateral hachydactyly of the middle phalanx of the fifth finger.

Discussion

Myositis ossificans progressiva is probably a congenital heredity mesodermal disorder. Approximately 260 cases have been reported (1). The disease is characterized by ossification of fascia, tendons, ligaments, striated muscles, apo-

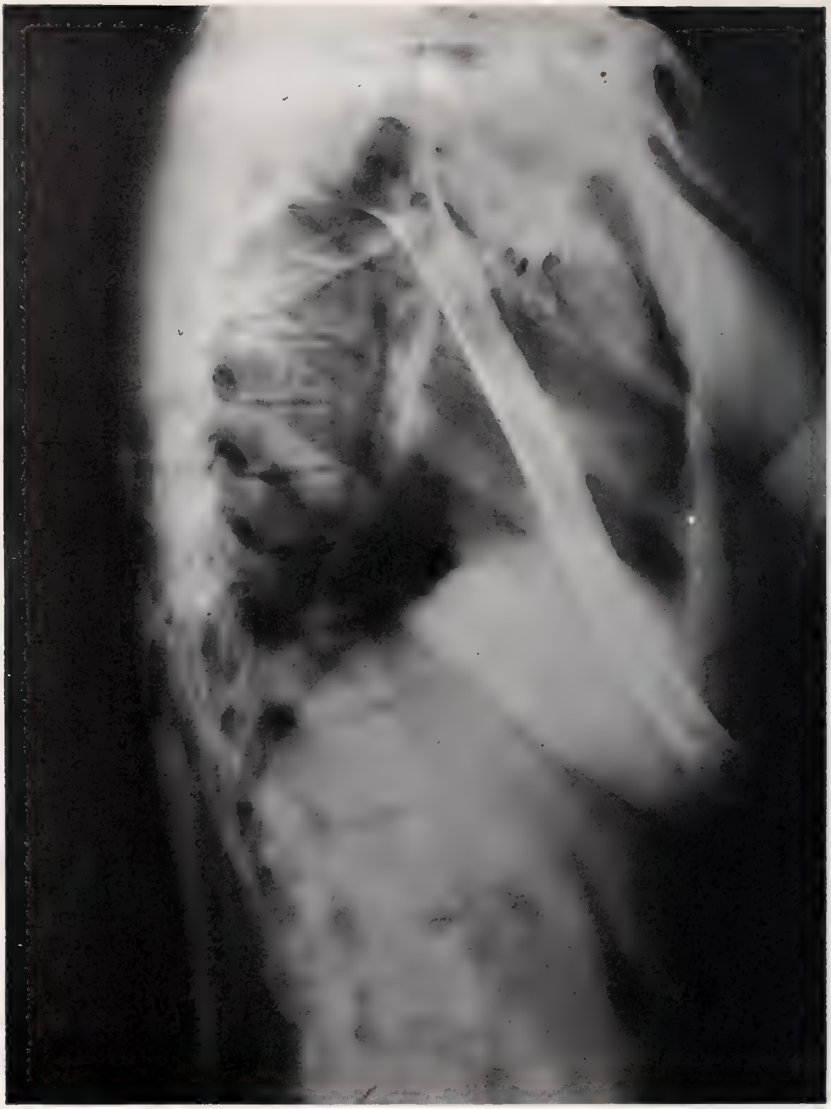
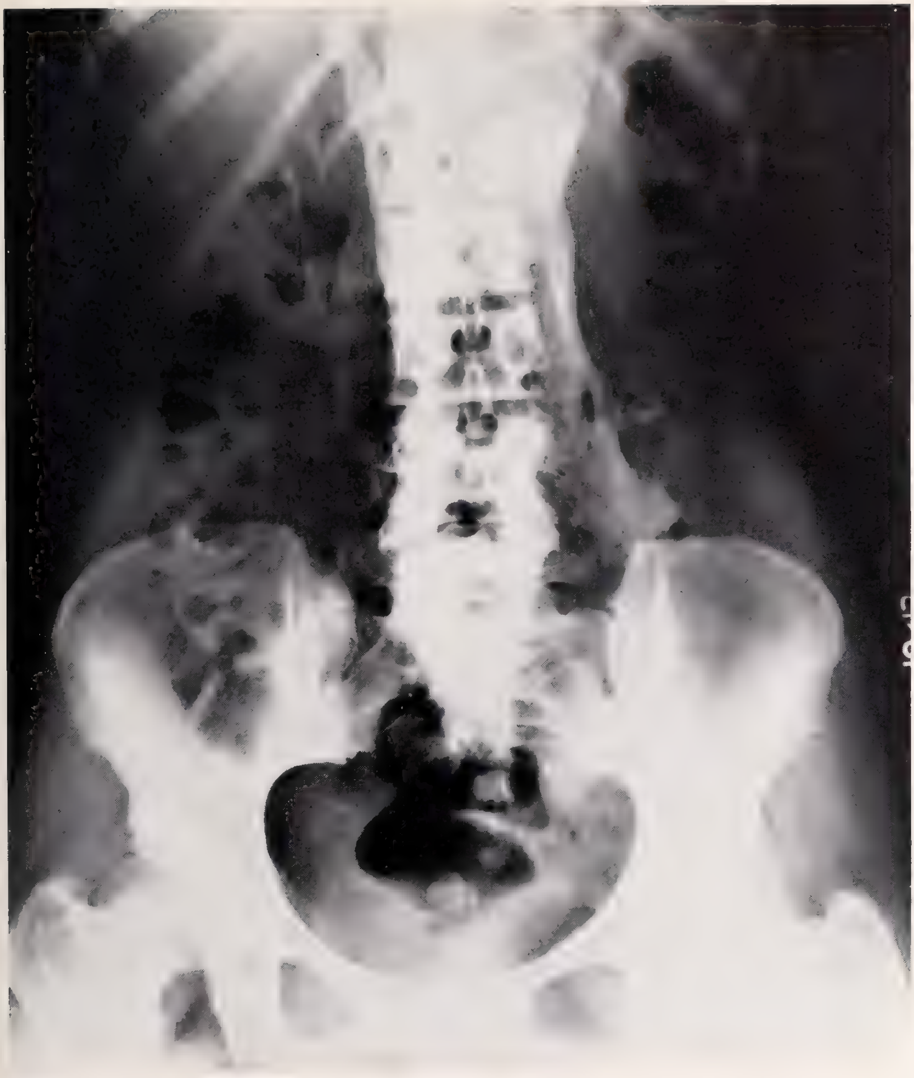


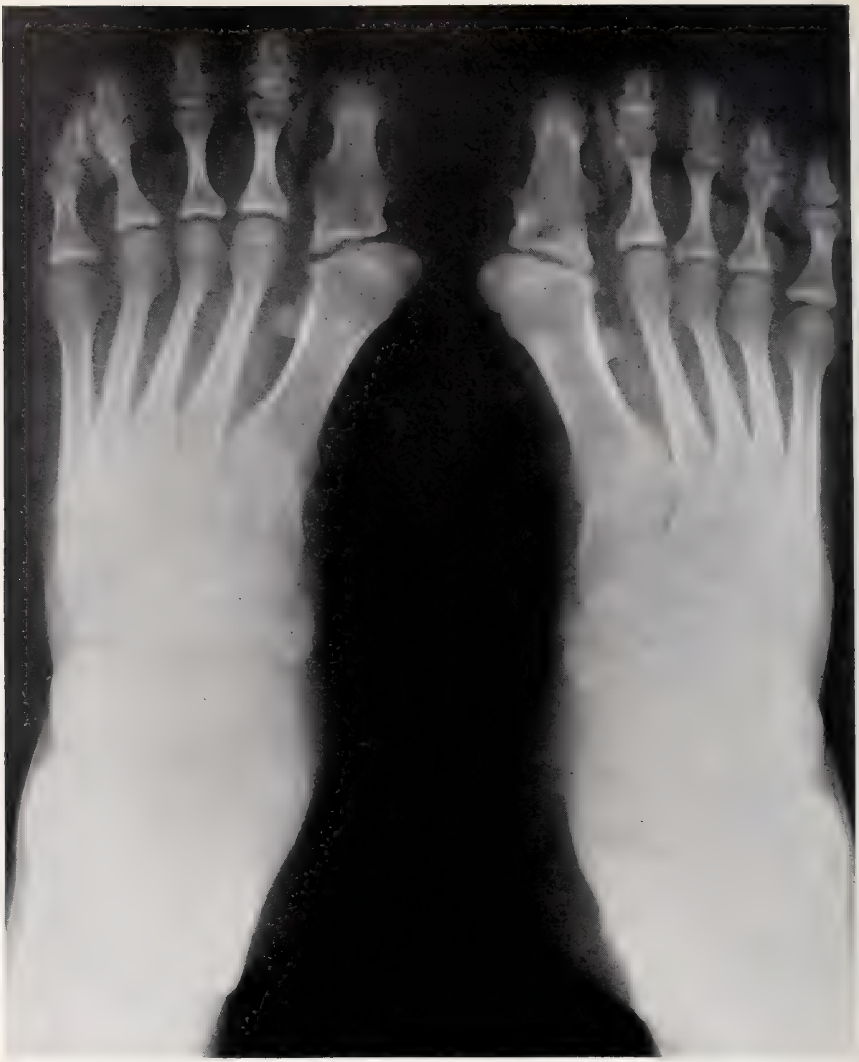
Fig. 1B. A lateral view of the chest demonstrates ossification of the paraspin musculature posteriorly along the soft tissue planes.

neuroses, and even of the skin. The muscles of the eye, tongu [illegible] phragm, larynx, and perineum are spared. Congenital anomalie [illegible] and feet are frequently associated. The most common deformities [illegible] microdactyly or adactylia, especially of the first metacarpals and phalanges of the thumb or great toe, and brachydactyly of the middle phalanx of [illegible] fifth digit. Other described deformities include: hallux valgus, exos [illegible] ear lobes, absence of the two upper incisors, spina bifida, and a "[illegible] [illegible]es"



Case 352, Fig. 2. Supine film of the abdomen discloses dense paraspinal and psoas muscle ossification mainly along the upper half of the back.

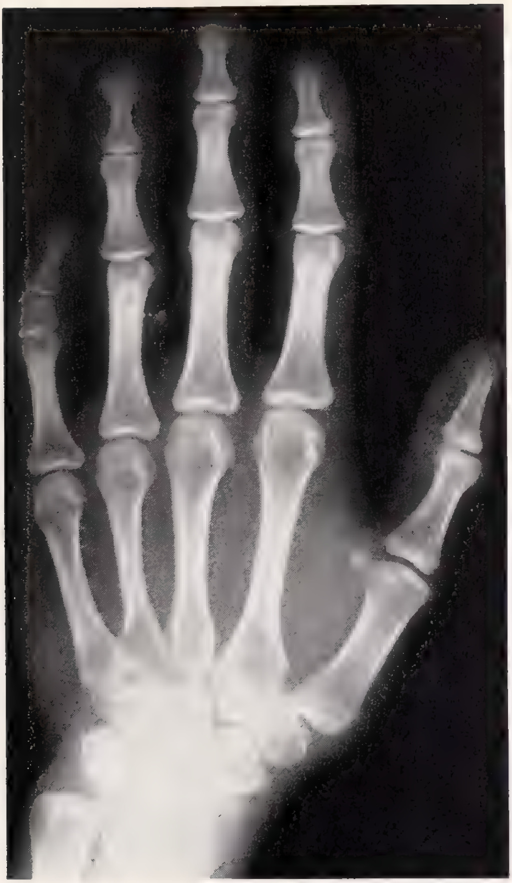
(2). Approximately 25 percent of the cases demonstrate no associated anoma- [illegible]gy is unknown; however, minor trauma may cause exacerbations [illegible] r susceptible individuals (3). The disorder is most often diag- [illegible] uring the first few years of life, occasionally even in infancy without a history of antecedent trauma. There is no sex predilection. There is an increased incidence among those of the same genetic linkage with reports in 2 sets of [illegible] twins (4, 5). The basic pathologic process is an interstitial myositis or [illegible] (6). Initially, there is extensive proliferation of the interstitial



Case 352, Fig. 3. Frontal view of both feet reveals fused distal phalanges of the first, third, fourth and fifth toes bilaterally. The first metacarpal is shortened, and there is a bilateral hallux valgus. A hypoplastic middle phalanx of the second toe is present.

connective tissue associated with little inflammatory cell reaction or hemorrhage. After a few weeks, the connective tissue condenses and produces osteoid. Occasionally cartilage formation may be an intermediate step. Spicules of normal bone are formed, and the ossification extends peripherally. Abnormal laboratory data may include eosinophilia (2, 7) and elevated alkaline phosphatase in biopsy specimens (8).

Often the first clinical manifestation is the appearance of doughy or firm



Case 352, Fig. 4. Frontal view of the left hand demonstrates brachydactyly of the middle phalanx of the fifth digit. A similar anomaly was present in the right hand.

subcutaneous masses about the dorsum of the neck and shoulders. The masses may be painful, hot and tender, rarely associated with fever. These masses gradually shrink as they collagenize and ossification finally ensues. New masses appear and the cycle is repeated. The shoulder, neck and spine are most commonly affected often with a resulting tilt of the head to one side and a dorsal kyphosis. The plantar and palmar fascia may ossify. Exostoses are often found at the attachments of fibrous structure to bone. Progressive involvement of the muscles of the back, extremities, abdominal wall, and intercostals continues until entire muscles or groups of muscles are converted into osseous tissues that acquire the shape of the involved muscle. Calcified bridges between adjacent muscles and across joints result in ankylosis. Usually, the articular surfaces of the joints are spared although the joint capsule may ossify. The final result is literally a "stone man". All joint motion is finally lost and the victim succumbs to intercurrent infection and inanitum. No effective treatment is known although steroids are used empirically.

Case Report: MYOSITIS OSSIFICANS PROGRESSIVA.

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PAGET'S DISEASE WITH TRANSVERSE CORTICAL FRACTURE

Submitted by
John S. Train M.D.

CASE NO. 353

This 78-year-old white woman was admitted to The Mount Sinai Hospital with a cerebral vascular accident. While in the hospital, Roentgen examination of the lower extremities was performed because of complaints of bilateral thigh pain. A frontal film of the thighs demonstrates lateral bowing of the femurs. A poorly defined area of radiolucency is seen bilaterally extending from the most distal margin of the bone to the mid-shaft region where it ends abruptly (Fig. 1A, 1B, large arrows). In the distal end of the right femur, there are areas of fluffy sclerosis associated with coarsening of the trabecular pattern and cortical thickening (Fig. 1A). Along the lateral aspect of both femurs (in the region of the most proximal extent of the disease) transverse, lucent cortical defects are seen (along small arrows).

Discussion

The course of Paget's disease can be divided into three stages. The first is the destructive stage; the second, the mixed stage; the third, the sclerotic stage. The first or destructive state is best demonstrated in the skull as osteoporosis circumscripta. It represents massive osteoclastic activity with reabsorption of the normal bone. It is seen most frequently in the long bones as a diffuse area of radiolucency starting at the distal margin of the bone and advancing proximally at various rates (Fig. 1). The active edge is often sharply demarcated and wedge-shaped, with the point of the wedge marking the farthest extent of the disease. The case presented is representative of this early stage.

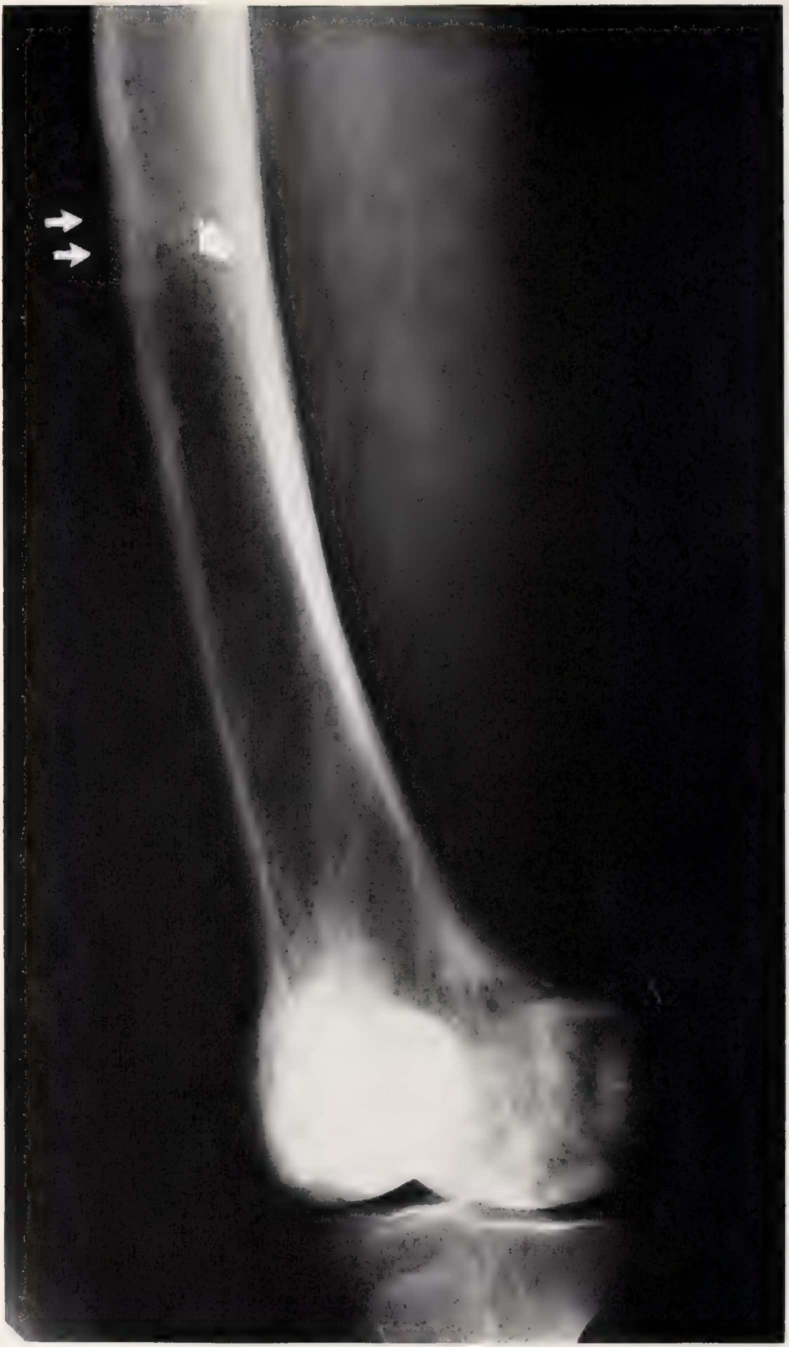
Pagetoid bone responds to stress in a greatly exaggerated manner. Torsion stresses cause the periosteum to become very active and to lay down new Pagetoid bone. Compression stresses greatly inhibit growth, and, in the region of compression forces, bone reabsorption occurs unopposed by new bone production. Bed rest causes massive reabsorption and diffuse atrophy in great excess to the response that would be expected for normal bone. Hypercalcemia can be a problem, causing stone formation and subsequent renal damage.

This excessive response to stress accounts for the deformity of Paget's disease. Weight bearing on the femur produces compression stress medially, and torsion stress laterally. These forces result in the stimulation of the periosteum laterally and the production of new Pagetoid bone in that region. Resorption of bone medially unopposed by new bone formation occurs. The result is lateral bowing. This process is also well demonstrated in the tibia where anterior torsion stresses and posterior compression stresses lead to anterior bowing. This mechanism is also believed to be responsible for other deformities in Paget's disease such as basilar invagination and inward protrusion of the acetabula (5).

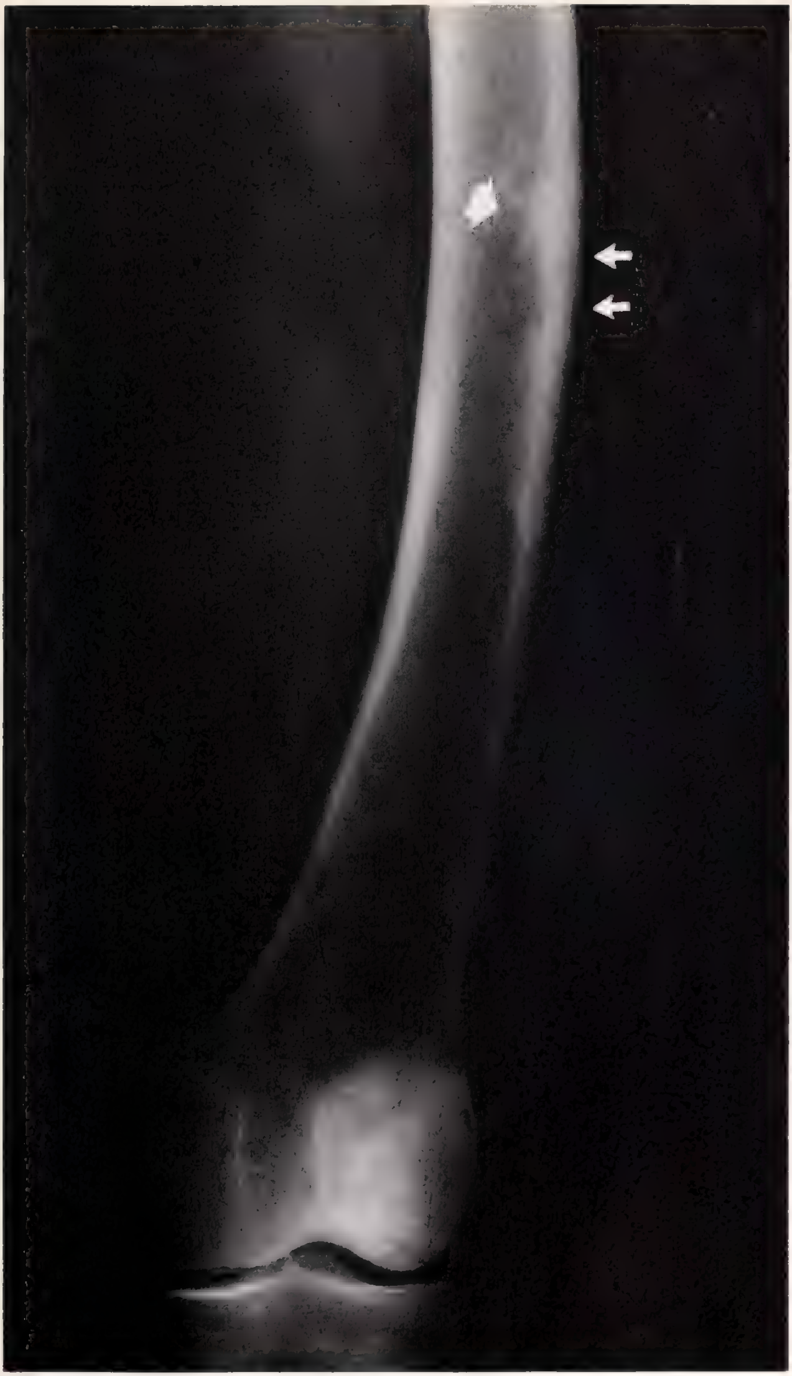
Pagetoid bone is susceptible to fracture. Collins put this incidence at about ten percent of all cases (1). As Pagetoid bone has no structural organization, the fractures follow the lines of stress as they are applied to the bone. Most trauma causes transverse stress to occur in the bone and therefore most pathological fractures are transverse. Stress fractures may involve the cortex only and appear roentgenographically as lucent defects (Fig. 1). In Paget's disease, they are described as occurring along the lateral aspect of the femur and the anterior aspect of the tibia, where torsion stresses occurs. They occur most often within the region of active disease, and often appear in rows almost equally distant from each other. Healing occurs by periosteal and endosteal growth.

The transverse cortical fractures of Paget's disease should be differentiated from the pseudo-fractures or Looser's zones described in osteomalacia. The latter are bilaterally symmetrical with specific locations that differ from those seen in Paget's disease. Whereas the fractures in Paget's disease occur laterally in the femur, Looser's zones occur along the medial aspect of the upper femur, the axillary border of the scapula, the ribs, and pubic rami. Steinbach feels that they are not fractures, but erosions secondary to constant pulsation by vessels which are in close proximity to the cortex (6). Pathologically, they consist of poorly ossified osteoid with no evidence of fracture. Transverse cortical fractures are also described in osteoporosis, osteogenesis imperfecta, hyperparathyroidism, and fibrous dysplasia. Radiologically, they are quite similar in appearance to the transverse fracture seen in Paget's disease and to Looser's zones. They can, however, be differentiated by examining the surrounding bones and by clinical correlation.

Case Report: PAGET'S DISEASE WITH TRANSVERSE CORTICAL FRACTURE.



Case 353, Fig. 1A and 1B. Frontal film of the thighs demonstrates lateral bowing of the femurs. A poorly defined area of radiolucency is seen bilaterally extending from the most distal margin of the bone to the mid-shaft region where it ends abruptly (large arrows). In the distal end of the right femur, there are areas of fluffy sclerosis



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associated with coarsening of the trabecular pattern and cortical thickening. Along the lateral aspect of both femurs (in the region of the most proximal extent of the disease) transverse, lucent cortical defects are seen (along small arrows).

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Surveillance of the Fetus During the Intrapartum Period

EBERHARD MUELLER-HEUBACH, M.D. AND KARLIS ADAMSONS, M.D., PH.D.

It has been estimated that three percent of all infants delivered annually in the United States are born with some degree of permanent neurologic deficit. Because increased prevalence of this condition has been found among infants born in a depressed state exhibiting signs of intrauterine asphyxia, concerted efforts have been made to develop methods for surveillance of the fetus during labor and delivery.

Factors influencing oxygen availability to the fetus

Although most fetuses experience some oxygen deprivation during the intrapartum period, only in a small fraction is the reduction in oxygen supply so severe as to affect adversely the physiologic performance of the fetus or the newborn. Because the fetus is not in a direct contact with the external environment its oxygenation is entirely dependent upon oxygen supply from the mother. The oxygen content of maternal blood and the flow rates through the intervillous space have to be of certain magnitude to permit diffusion of sufficient amounts of oxygen across the placenta into the umbilical circulation to meet the requirements of fetal tissues. During uterine contractions the perfusion of the intervillous space is interrupted at relatively low elevations of intrauterine pressure above the resting tonus of the uterine muscle. The concomitant interruption of oxygen supply to the fetus is tolerated during normal labor due to the amount of oxygen stored in the intervillous space blood and the fetal circulation. In the well-oxygenated rhesus monkey fetus these oxygen stores have been found to be sufficient to maintain vital signs for about one minute after complete interruption of intervillous space perfusion. It becomes apparent that the essential phase during labor is the adequate relaxation of the uterine muscle between contractions to allow restoration of intervillous space perfusion. Elevation of the "resting tone" of the uterus is more detrimental to the fetus than frequent uterine contractions of high amplitude, provided that the intervillous space perfusion is restored during the periods between contractions. Reduction of flow rate through the intervillous space and that of the oxygen content of the arterial blood of the mother may cause oxygen deprivation of the fetus even in the presence of normal labor. Compression of inferior vena cava, aorta and iliac arteries by the uterus during labor in a supine position may diminish the perfusion of the intervillous space to an extent which produces fetal asphyxia

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From the Department of Obstetrics and Gynecology, College of Physicians and Surgeons of Columbia University, New York, N.Y. 10032; and the Departments of Obstetrics and Gynecology and of Pharmacology, Mount Sinai School of Medicine of The City University of New York, N.Y. 10029.

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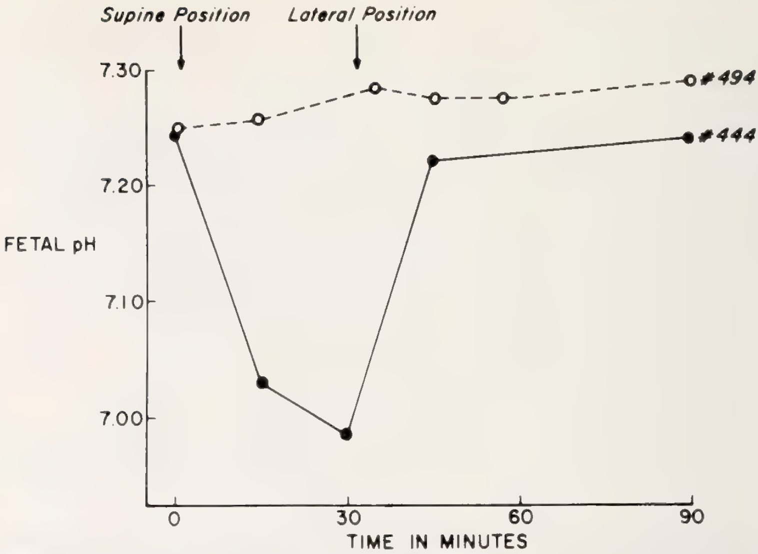


FIG. 1. Effect of maternal position on pH of arterial blood in two fetal rhesus monkeys near term (Courtesy of Pan American Health Organization).

(Fig. 1) (1, 2). Pharmacologic agents which interfere with the activity of the autonomic nervous system apparently aggravate this situation. Maternal dehydration and hypovolemia is known to have a similar effect (3). This also pertains to hypotension from spinal anesthesia, deep general anesthesia or blood loss. The actual reduction in uterine perfusion may be more pronounced than is indicated by the fall in systemic blood pressure since alterations in regional blood flow are not necessarily reflected in systemic blood pressure. Expansion of the circulatory volume of the mother by intravenous infusion of liquids increases uterine perfusion and ameliorates the fetal condition (Fig. 2). Our recent studies in the subhuman primate have indicated that a prolonged increase in the concentration of catecholamines in maternal blood markedly impairs fetal oxygenation. This is brought about by vasoconstriction in the uterine circulation (4). In a number of cases fetal condition continued to deteriorate after termination of catecholamine infusion to the mother due to a transient postinfusion hypotension (Fig. 3).

It should be noted that the tolerance of the fetus to a given duration of asphyxia is not constant. It decreases with increasing maturity of the fetus as a whole, but particularly with that of its central nervous system. A fetus with hyperthyroidism is expected to be less tolerant to deprivation of oxygen than the normal fetus or one that suffers from hypothyroidism. A fetus lacking major portions of the central nervous system (anencephalic or hydranencephalic) is known to be exceptionally tolerant to interference in oxygenation because of its low metabolic requirements. The fetus suffering from erythroblastosis is more likely to suffer from asphyxia during the course of labor. This is not due to an intrinsic susceptibility but to a diminished volume of the intervillous space and a reduced oxygen content of fetal blood.

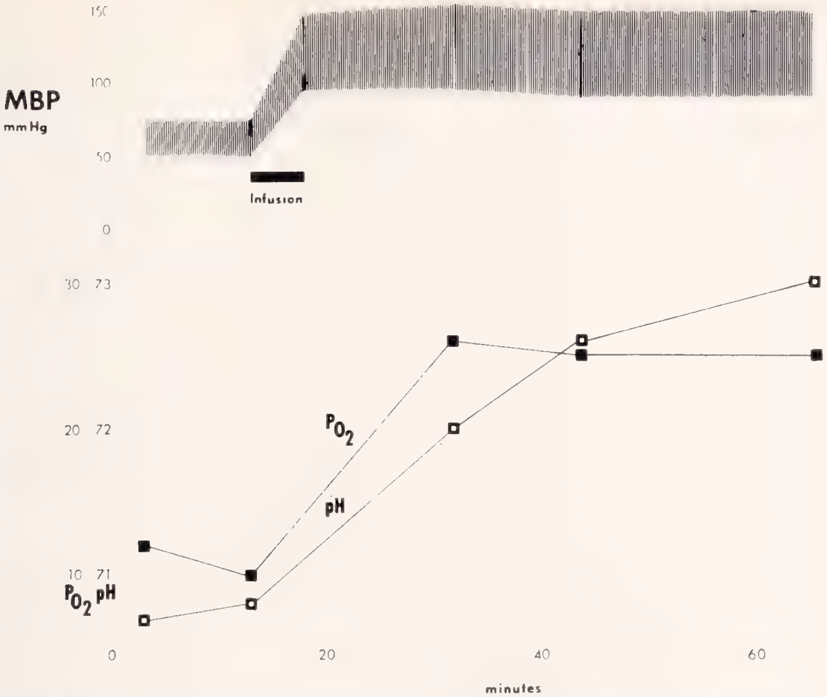


FIG. 2. Maternal blood pressure and pH and P_{O_2} of arterial blood of the fetus during saline infusion into a hypovolemic monkey mother near term (Courtesy of 26th Mexican Congress of Gynecology and Obstetrics).

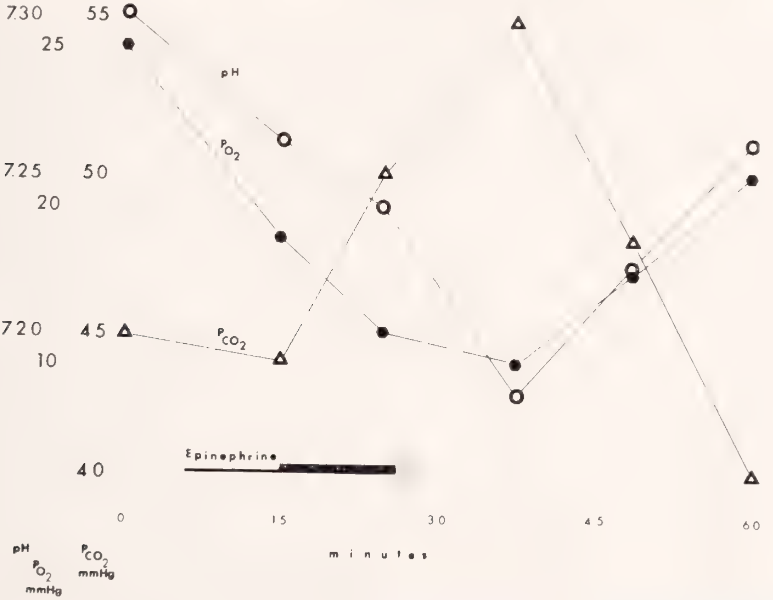


FIG. 3. Arterial blood pH, P_{O_2}, and P_{CO_2} of the monkey fetus during intravenous administration of epinephrine (1.3 and 3.7 mg per kilogram per minute) into the maternal circulation. Maternal hypotension was present for 15 minutes after the termination of infusion (Courtesy of American Journal of Obstetrics and Gynecology).

Assessment of the condition of the newborn

Most obstetricians have adopted the scoring system of Apgar to assess the condition of the newborn during the first few minutes of life. In this system heart rate, respiratory effort, muscle tone, reflex irritability and color of the newborn are graded with numbers from 0 to 2. The sum of these five numbers is used as an indicator of the condition of the newborn. Due to the widespread use of the Apgar scoring system and the frequent assumption that low Apgar scores are exclusively the result of asphyxia during the intrapartum period, it is important to ascertain the limitations of this system. The merits of the currently available methods to assess the condition of the fetus during labor and delivery may be misunderstood if they are evaluated on the basis of the Apgar scoring system. It has to be recognized that low Apgar scores may not only be the result of intrapartum asphyxiation of the fetus but also of hypnotic and analgesic agents. Pharmacologic agents which reduce the oxygen consumption of fetal tissues are beneficial under circumstances in which fetal availability is reduced. In newborn rhesus monkeys which were subjected to total asphyxia before the first breath, the time to the last gasp could be extended by 20 percent by administration of barbiturates (5). Our own experimental work revealed a reduction in oxygen consumption of similar magnitude in juvenile rhesus monkeys following the administration of 35 mg/kg of sodium pentobarbital (6). Newborns which did receive barbiturates during labor and delivery had low Apgar scores although they were not asphyxiated as judged by biochemical analysis. It is important to differentiate asphyxial depression from that induced by drugs when analyzing the relationship between the Apgar score and the neurologic status of the offspring.

Indicators of fetal condition during labor and delivery

The selection of an ideal indicator of fetal condition requires a variable which represents a vital function of the fetus. The time interval between a deviation of a chosen variable from normality and the occurrence of irreversible damage to cell function has to be sufficient to allow reversal of the adverse circumstance, or removal of the fetus from an unfavorable environment. The presently available methods of ascertaining fetal circumstance during labor and delivery can be divided into biochemical and biophysical ones.

Biochemical indicators of fetal condition

Oxygen deprivation of fetal tissues provokes biochemical changes in the intra- and extracellular environment among which an increase in hydrogen ion concentration, carbon dioxide tension and base deficit and a fall in oxygen tension are prominent. These intra- and extracellular changes are reflected in blood since equilibration between tissues and blood is rapid and blood flow to organs with high energy transformation rates (myocardium, CNS) constitutes a relatively large proportion of cardiac output. Under conditions of asphyxia these proportions are even increased, as has been found recently in the asphyxiated fetal rhesus monkey (7). Hence, blood is suitable as a source to gain

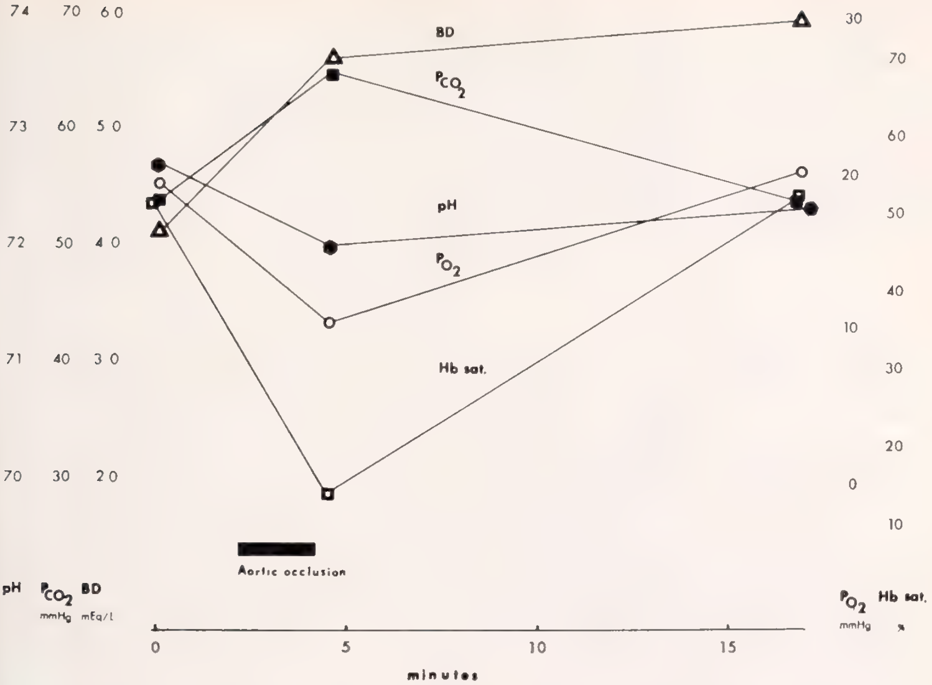


FIG. 4. Changes in pH, P_{O_2}, P_{CO_2}, base deficit and hemoglobin saturation with oxygen after interruption of intervillous space perfusion for two minutes by means of an occlusion of the abdominal aorta of the monkey mother (Courtesy of C. V. Mosby Company, St. Louis).

information about biochemical changes at the cellular level. The changes in acid-base state and oxygenation of arterial blood of the fetal monkey during asphyxia are illustrated in Figure 4. It can be seen that the tensions of oxygen and carbon dioxide change rapidly during asphyxiation. The high time-resolution of these variables is a disadvantage regarding their use as indicators of fetal asphyxia by a technique which depends upon intermittent sampling, because they return rapidly to preasphyxial levels after an asphyxial episode, and, thus, do not indicate previous disturbances in oxygenation. In addition, the oxygen content of blood is correlated not only with P_{O_2} but also with hydrogen ion concentration. The determination of base deficit in fetal blood as an indicator of fetal oxygen availability has not gained much popularity since it is time consuming and less accurate than the quantitation of hydrogen ions. The principal value of the determination of base deficit is that it allows one to identify antecedent episodes of asphyxia no longer detectable by pH measurement. From a clinical point of view, hydrogen ion concentration or its negative logarithm (pH) is the most satisfactory indicator of fetal oxygenation during the intrapartum period.

Blood from the fetus is obtained according to the technique developed by Saling (8). With the patient in a recumbent position an endoscope with an

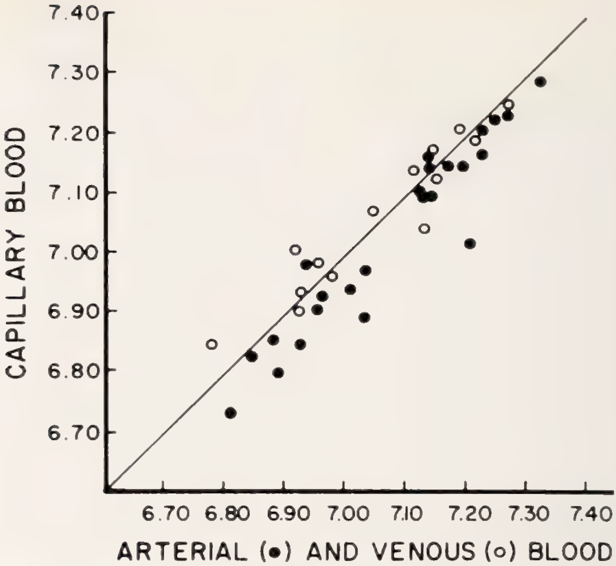


FIG. 5. Relationship between pH of arterial, venous and capillary blood from the presenting part of the monkey fetus during labor (Courtesy of Springer-Verlag, New York).

attached light source is introduced into the cervical canal. The presenting part of the fetus is identified and a small stab incision is made with a special blade protruding 2 mm. Blood is collected in long, heparinized tubes by capillary action. Complete determination of the various constituents reflecting fetal oxygenation requires only 0.2 to 0.3 ml.

Close correlation has been found between pH of capillary blood from the presenting part of the fetal monkey and that of the carotid artery and jugular vein (Fig. 5) (9). In the human the exact value of pH of fetal blood before the onset of labor is not known. On the basis of indirect evidence it is assumed to be about 7.35. In clinical practice it has become customary to regard a pH value of fetal capillary blood of less than 7.35 but more than 7.25 as innocuous, values from 7.20 to 7.25 as potentially hazardous and those below 7.20 as incompatible with fetal safety. The presence of toxemia, diabetes, HCVD, postmaturity and irregular fetal heart or deviations from the normal range of fetal heart rate are considered indications for biochemical assessment of fetal condition. In the normal patient the first blood sample is obtained when clinical signs of fetal distress appear. In the presence of conditions predisposing the fetus to asphyxia, sampling is initiated during the early phase of established labor irrespective of the presence of normal fetal heart rate. If the value of pH is above 7.25 a second sample is taken during the second stage, assuming that there are no new indications, or earlier if the initial pH was below 7.25 or the fetal heart rate abnormality persists. In cases with an initial pH below 7.25 fetal blood sampling is repeated as soon as possible. If the repeat sample gives evidence of progressive fetal asphyxia with pH values falling below 7.20, a decision in favor of rapid operative delivery of the fetus is made.

Ideally all fetuses should be supervised during labor by biochemical methods in order to eliminate asphyxiation of fetuses to a degree which irreversibly damages cell function. The major drawback of the biochemical method of fetal surveillance during labor is the necessity to remove the specimen for determination. This makes continuous assessment of fetal condition impossible. However, compared to biophysical methods of fetal surveillance the biochemical method is a more sensitive indicator of disturbances in fetal oxygenation and is relatively independent from compensatory influences.

Biophysical indicators of fetal condition

Fetal heart rate. Recording of fetal heart rate is the most frequently used biophysical method for fetal surveillance during labor and delivery. The reasons for selecting the performance of this organ as an indicator of fetal well-being are the fetal heart's high metabolic requirements and the fact that in the presence of reduced availability of energy a change occurs not only in cardiac output but also in the frequency of myocardial contractions. According to the technique devised by Hon (10) a small silver electrode coated with silver chloride is attached to the presenting part of the fetus and the QRS-complexes of the fetal electrocardiogram are used to trigger a cardiotachometer. The heart rate is displayed continuously by a recording polygraph together with the pressure within the uterine cavity obtained by means of an open-end catheter attached to a pressure transducer. A certain beat-to-beat irregularity characterizes normal heart rate which is thought to represent a continuous interaction between sympathetic and parasympathetic nervous systems. Three specific patterns of changes in fetal heart rate have been identified and are designated according to their temporary relationship to uterine contractions as "early," "late" and "variable" decelerations. This latest terminology replaces the previous synonyms for early deceleration, type I dip, early or V-shaped bradycardia; and for late deceleration, type II dip, late or U-shaped bradycardia. Early deceleration is thought to be innocuous for the fetus since no changes in biochemical composition of fetal blood are observed when this type of fetal heart rate change is of the usual short duration. The deceleration occurs at the time of the uterine contractions and usually lasts less than 30 seconds. It is caused by compression of the fetal head and is mediated through the vagus nervus. Compression of the fetal head leads to an increase in intracranial pressure which causes an increase in blood pressure of the fetus and activation of baroreceptor mechanisms. To what extent fetal bradycardia can be produced by head compression without a concomitant increase in intracranial pressure remains to be elucidated. Administration of atropine reduces but does not abolish the decrease in heart rate synchronous with uterine contractions.

Late deceleration is a result of a decreased activity of the cardiovascular centers of the central nervous system and the heart itself, necessitated by a reduction in the availability of energy. It appears late in the contraction phase and is maximal approximately 40 seconds after the peak of a normal uterine contraction (Fig. 6). This interval is the same as that observed in experimental studies in the subhuman primates characterizing the period between the peak of

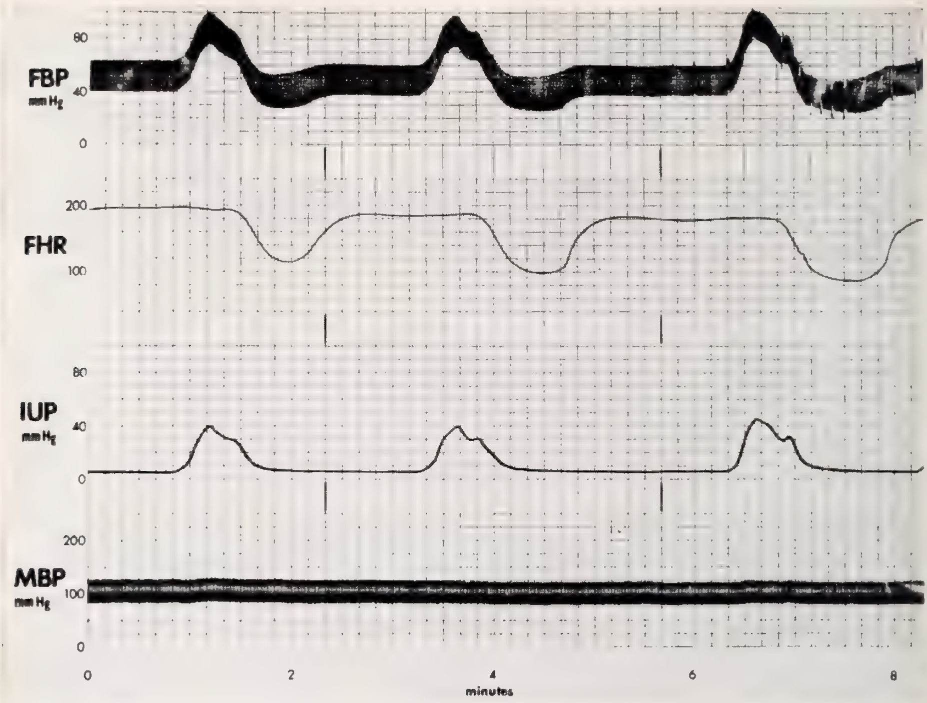


Fig. 6. Changes in heart rate and blood pressure of a chronically asphyxiated monkey fetus following uterine contractions ("late decelerations") (Courtesy of C. V. Mosby Company).

the uterine contraction and the moment at which blood samples from the arterial side of the fetal circulation have the lowest value of oxygen tension and oxygen content. Recent work on the rhesus monkey has demonstrated that late deceleration is accompanied by fetal hypotension (11). It is inferred, although not yet experimentally established, that bradycardia and hypotension represent a decrease in cardiac output. This is, however, quite probable since fetal asphyxia and acidosis are known to be accompanied by an appreciable reduction in fetal cardiac output.

"Variable" decelerations are characterized by their occurrence at any phase of a uterine contraction. It has been proposed that they are due to compression of the umbilical cord. Hence, elevation of the fetal head or change of maternal position frequently make this pattern of heart rate disappear. Impairment of fetal oxygenation has been found in cases of "variable" deceleration of moderate to severe degree.

Apart from the electrical activity of the fetal heart, two other phenomena have been used for the monitoring of fetal heart rate. They are movement of blood in the heart and major arteries, and heart sounds. The first is detected by ultrasound, taking advantage of the Doppler principle which states that the frequency of a reflected sound wave is altered when the reflecting medium changes its position in relation to the source of sound wave emission. Recently developed transducers having a cross-sectional area of the sound beam of nearly 400 mm^2, and a penetration depth of 6 to 10 cm have proven to be very satisfactory for this purpose. The attractive feature of this technique, compared to that of resorting to the detection of fetal ECG, is the fact that the transducer is applied on the abdominal wall of the mother and not on the presenting part of the fetus. Thus continuous monitoring of fetal heart rate can be initiated before dilatation of cervix and rupture of amnion. External application of the device also eliminates the need for highly skilled manpower for its utilization.

The biologic effects of ultrasound on tissues are chiefly those of heat, and the energy levels used for the monitoring of fetal heart rate are so low that even a ten- to 100-fold increase would appear to be of no consequence.

It is projected that with further refinement in instrumentation this technique will receive wide application in fetal surveillance during labor.

The sonic waves emitted by the fetal heart have been found to be less satisfactory for monitoring purposes by electronic means. This is due to external and internal noise and the fact that the characteristics of frequency, amplitude and duration of heart sounds are rather unsuitable for the identification of a single event during a cardiac cycle by a differentiating circuit.

Changes in fetal heart rate are a function of a variety of factors. Fetal heart rate can be affected by direct stimulation of the central nervous system, by humorally transmitted substances or by a reduction in oxygen availability. We have found in the rhesus monkey that cardiovascular performance of the fetus is less responsive to catecholamines than that of the adult (4). Furthermore, our studies revealed that the baseline fetal heart rate of the rhesus monkey is maintained within normal limits over a wide range of hemoglobin saturations with oxygen (Fig. 7). Unless hemoglobin saturation with oxygen of the arterial blood of the fetus was below 25 percent, no unequivocal fall in the baseline heart rate was present. Baseline fetal heart rates were also maintained over a wide variety of hydrogen ion concentrations (Fig. 8). Only in severely acidotic fetuses was there a marked fall in the baseline fetal heart rate. Using intermittent interruption of the intervillous space perfusion by means of aortic occlusion in the subhuman primate as a model to examine the conditions under which late decelerations occur we found that oxygen tension has to be lowered below 25 mmHg and pH below 7.20 before late deceleration appears (12). The relative stability of fetal heart rate during conditions of asphyxia can be partly accounted for by the relative increase in the proportion of cardiac output received by the heart under conditions of asphyxia. Thus, it has to be realized that late deceleration is a late indicator of changes in fetal oxygen availability which appears after compensatory mechanisms have failed to maintain cardiovascular performance of the fetus. Work is in progress to investigate in the subhuman primate whether late deceleration can be used as an indicator to characterize a degree of fetal asphyxia from which recovery without brain damage is anticipated.

Fetal electrocardiogram. In order to ascertain the potential value of the

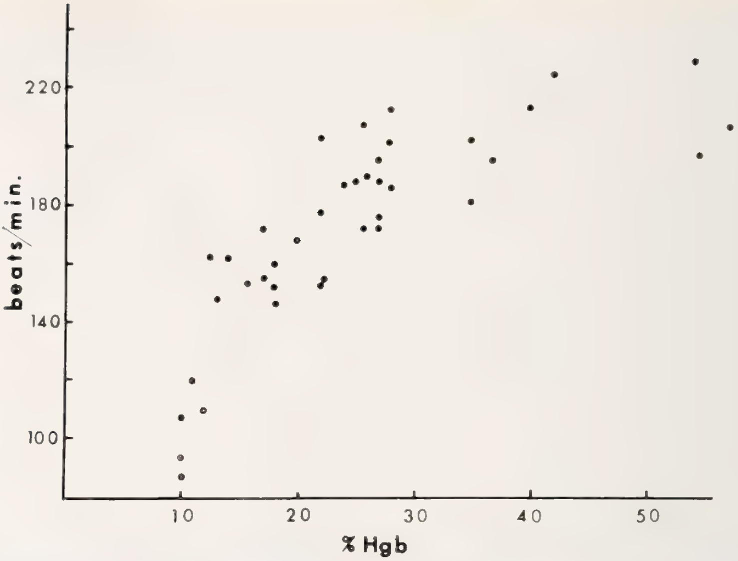


Fig. 7. Relationship between heart rate of the mature monkey fetus and hemoglobin saturation with oxygen of arterial blood.

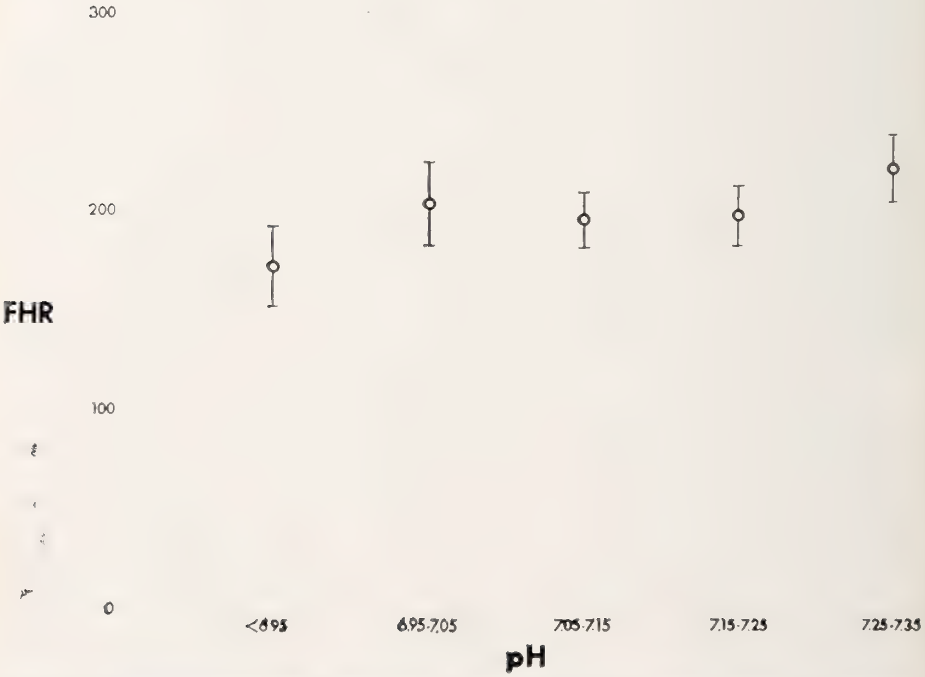
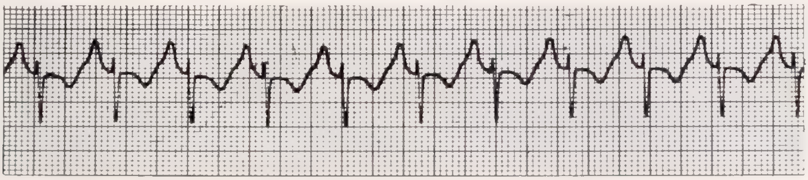
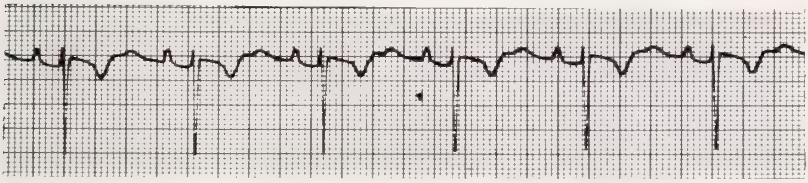


Fig. 8. Relationship between heart rate (mean ± S.E.) of mature monkey fetuses and pH of arterial blood (n = 9 to 15).

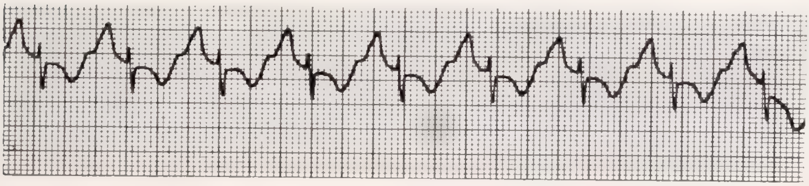
electrical activity of the fetal heart as a method to assess fetal condition during labor and delivery we have examined changes in fetal ECG of the rhesus monkey with electrodes attached to standard lead positions and to the scalp during different states of fetal oxygenation. This enabled us to obtain optimal electrocardiographic recordings. In clinical practice when the ECG signal is obtained from the presenting part of the fetus it is necessary to use computer averaging techniques in order to minimize the distortion of the ECG signal by other bioelectric events. According to our studies the "normality" of the fetal electrocardiographic signal is difficult to define because of vast individual differences. Changes in ECG can be ascertained only if a baseline ECG has been obtained at a time when the fetus was known to be in good condition. Thus, each fetus has to serve as its own control. During elevations in intrauterine pressure changes in the fetal ECG signal may be observed which are most likely caused by transient alterations in the position of the electrical axis of the fetal heart. Although changes in the electrical activity of the fetal heart during acute asphyxia may be readily apparent, the changes observed during chronic asphyxia are much less conspicuous, and a state of severe fetal compromise may develop without remarkable changes in the electrical activity of the fetal heart (Fig. 9). In view of these considerations it is envisaged that the application of



Initial ECG



ECG during chronic asphyxia



ECG during acute asphyxia

Fig. 9. Electrocardiogram of a monkey fetus near term before asphyxia (pH = 7.30, P_{O_2} = 23 mmHg), during acute asphyxia (pH = 7.315, P_{O_2} = 13 mmHg) and during chronic asphyxia (pH = 7.02, P_{O_2} = 11 mmHg) (Courtesy of C. V. Mosby Company).

fetal electrocardiography as a diagnostic method for the detection of fetal asphyxia will be limited.

Fetal electroencephalogram. The electrical activity of the fetal brain has been investigated as an indicator of fetal asphyxia in the human and in several species of animals. The signal-to-noise ratio, however, has been found to be low even after applying special electrodes and averaging by computer. A study of the fetal EEG in sheep has revealed that unequivocal changes in the wave pattern are elicited only at oxygen tensions barely above those leading to a complete disappearance of the electrical output of the fetal brain (13). In the human fetus the amplitude of brain potentials is much smaller than in sheep and, hence, the evaluation of changes even more difficult. So far no study has been made to correlate changes in electrical activity of the fetal brain to changes in acid-base state, oxygenation or cardiovascular performance. From the evidence accumulated to date it does not appear that fetal electroencephalography is a useful method for fetal surveillance during the intrapartum period. Preliminary studies using brain potentials evoked by auditory stimuli indicate that fetal oxygen deprivation alters the wave pattern, and the interval between stimulus and response is prolonged (14). This technique appears more promising than the use of the random electroencephalogram alone.

Conclusion

Possessing a more complete understanding of factors influencing fetal oxygenation, and being armed with new methodology and advanced instrumentation, the present-day obstetrician can offer his intrauterine patient during the course of labor a hitherto unprecedented surveillance. Biochemical analyses of fetal blood for constituents reflecting fetal oxygenation provide reliable information regarding the availability of energy to vital tissues of the fetus. Among the various indicators pH has proven to be the most useful in clinical practice. Extensive experience with fetal blood sampling has established that the procedure is safe and readily performable by a trained individual. It is also known that change in the composition of fetal blood precedes any measurable change in the physiologic functions and irreversible structural changes at either cellular or organismic levels. Until the time when suitable electrodes are developed for measurement of oxygen and CO_2 tensions in tissues, the intermittent nature of the observation process will remain as a shortcoming for all biochemical techniques used in the surveillance of the fetus during labor. Among the biophysical techniques, continuous monitoring of fetal heart rate offers the most promise. The use of an external detector which utilizes high frequency sound is likely to broaden the indications and the applicability of continuous heart rate monitoring during the conduct of labor. The shortcoming of fetal heart rate as an indicator of fetal oxygenation is its inability to reflect early changes in oxygen availability.

At present a combination of biochemical and biophysical methods for assessment of fetal condition during labor and delivery appears to be the most promising approach for the elimination of brain damage due to intrapartum asphyxia.

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Chronic Left Heart Failure—An Experimental Model in the Dog

RICHARD P. LASSER, M.D., JACOB I. HAFT, M.D.,
BERTRAM J. NEWMAN, M.D., DOUGLAS F. ALLEN, M.D.,
JUNISHI ISHIGURA, M.D., AND CHARLES K. FRIEDBERG, M.D.

This communication will report on the development in the dog of an experimental preparation demonstrating chronic progressive left heart failure for the purpose of studying sequential hemodynamic changes and interrelationships between cardiovascular abnormalities and renal function (1, 2).

The difficulty with the development of a chronic preparation is that the sudden imposition of a lesion designed to decompensate the normal left ventricle must be of such a nature that it does so progressively and over a protracted period of time and does not cause death precipitately. On the other hand, a lesion which is less than rapidly lethal, induces compensatory mechanisms and cardiac hypertrophy and the animal is liable to return to stable and relatively normal cardiac dynamics. Thus, the line is a very fine one between an overwhelming defect and inadequate one. Because of this fact and because of the difficulty with precise quantification of a surgically produced effect, the yield of animals available for study who show the desired degree of failure is necessarily variable and is a small percentage of the total operated and studied, no matter what lesion or combination of lesions is selected. After unsatisfactory experiences with surgically induced mitral insufficiency, aortic insufficiency or stenosis, a left subclavian artery to left atrial shunt was developed, providing a controlled diastolic overload of the left ventricle (3). This lesion caused chronic elevation of left ventricular diastolic pressure, left atrial and pulmonary capillary pressure, cardiac hypertrophy, and electrocardiographic changes of left ventricular hypertrophy. However, despite chronic elevation of left heart diastolic pressure, these animals did not progress to pulmonary edema and did not show reduction of resting systemic blood flow; they showed a normal glomerular filtration rate and renal plasma flow and no deficit in the excretion of a sodium load. Therefore, in order to further increase the cardiac stress, the current preparation was developed wherein the left subclavian artery to left atrial shunt was combined with ligation of one or two of the left ventricular branches of the left anterior descending coronary artery. These lesions are created during a single surgical procedure. This communication will report on hemodynamic studies and observations in a group of eight surviving animals with this combination of lesions. From the data obtained we feel that this is the first successful model of isolated left heart failure in the dog.

From the Department of Medicine, Division of Cardiology and the Department of Surgery, Division of Cardiothoracic Surgery, The Mount Sinai Hospital, New York, N. Y. 10029.

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Material and Methods

Operations were performed on eleven adult dogs, 16 to 22 kilograms, and eight survived the operation and the immediate postoperative period. Each was subjected to right and left heart cardiac catheterization, performed under chloralose-urethane anesthesia both prior to operation and between one and two weeks after surgery. Three long-term surviving animals were studied at intervals thereafter, for up to twenty months observation period. Statham transducers, P23D, were used and recordings were made on a multi-channel oscilloscopic recorder. Systemic cardiac output determinations were performed in duplicate, utilizing measurement of oxygen consumption and arteriovenous oxygen content in a Van Slyke apparatus. Technical details have been previously reported (3). The operative procedure consisted of establishing a shunt between the left subclavian artery and left atrial appendage by means of a Teflon® graft 6 mm in diameter. The superior and inferior anterior left ventricular branches of the left anterior descending coronary artery (below the perforating septal branch) were then freed and sutures placed about their origin. Fifteen minutes after the opening of the shunt and after the cardiac function had stabilized, the initial coronary artery branch was ligated. If the area of ischemia which developed appeared to measure about 2 × 2 cm of the anterior surface of the left ventricle, then only one branch was occluded. If not, the second branch was then ligated. Continuous electrocardiographic monitoring was performed. During the recovery period, the animal was given 60 mg of quinidine hydrochloride intramuscularly three times a day for three days and fed a low sodium diet (14 mg of sodium per 100 gr). Following operation, dogs were observed and weighed daily. Daily electrocardiograms were taken and the chest was ausculted for the characteristic presence of a to-and-fro machinery murmur which indicated shunt patency. All dogs reported in the current series manifested shunt patency during the entire period of observation. A response to simulated exercise was studied in a series of normal animals and in three of the postoperative animals one month following operation. Electrical exercise was simulated in the anesthetized animal by electrical stimulation of the hind muscles through needle electrodes in two limbs employing a Grass Stimulator at 80 volts, stimulus duration 5 msec and 4 shocks per second (4). At the end of ten minutes of study exercise, intracardiac pressures were recorded, oxygen consumption measured, and blood samples drawn from right ventricle and femoral artery for oxygen content to determine the systemic blood flow.

The response to digitalis administration of intracardiac pressures and systemic blood flow was tested postoperatively in three surviving dogs by intravenous administration of single doses of ouabain, 0.4 mg or 0.6 mg. The total exchangeable sodium space was determined in nine normal dogs and in three long-term surviving animals using Na^{24}. Dogs were kept in a metabolic cage for 24 hours and counting was done on serum and urine in a well-type scintillation counter and pulse height analyzer. Postmortem examinations were performed in all animals to verify the patency of the shunt, to determine heart size, presence or absence of pulmonary edema, and extent of myocardial infarction.

Results

The operative survival of these dogs with arterial-left atrial shunt and myocardial infarction was excellent in that eight of eleven operative animals survived the immediate postoperative period and five animals survived for two months to twenty months with marked elevation of left ventricular end diastolic pressure, showing that this highly abnormal hemodynamic state could be tolerated and, in fact, was progressive. During the immediate postoperative period, ventricular arrhythmias were frequent but by the third postoperative day, regular sinus rhythm had usually returned. Postoperatively a continuous systolic and diastolic machinery-like murmur was audible in all animals, indicating patency of the shunt. Clinically, animals who eventually developed pulmonary edema appeared listless, failed to eat as well as the others, and showed tachypnea at rest early in the postoperative period. Rales were audible in lungs of three such animals just prior to death. The electrocardiograms taken postoperatively at one week showed evidence of myocardial infarction with abnormal Q-waves in one or more leads from V-3 through V-7 and occasionally in leads I and AVL in all animals. Table I shows the preoperative and early postoperative hemodynamic findings, the eventual fate of the eight animals, and long-term follow-up catheterization studies in three dogs. Four of the animals—Nos. 6586, 6881, 7392, and 7626—developed acute pulmonary edema on the 12th, 13th, 20th and 42nd postoperative day respectively. Three of these dogs died in pulmonary edema. Animal No. 7626 was treated acutely with ouabain intravenously and chronic digitalization. The pulmonary edema subsided, the animal survived for nineteen months. Four other animals survived for protracted periods without evident pulmonary edema and were sacrificed at the end of the periods noted on the chart.

The hemodynamic data comparing preoperative with the postoperative values obtained within the first two weeks show that the essential aim of the preparation is achieved in that a considerable increase in left ventricular end-diastolic pressure (LVEDP) has been produced with a value rising from an average of 7.9 mm Hg preoperatively to 21.1 mm Hg postoperatively. The range of preoperative LVEDP is from 5.1 to 11.2 while the range of values observed postoperatively is 14.0 to 31 mm Hg. The marked rise in LVEDP is not accompanied by any significant change in left ventricular systolic pressure as the preoperative value is 164.5 mm Hg and postoperatively 169.5 mm Hg. Right ventricular pressures show that there has been a small average rise postoperatively in systolic pressure from 40.4 to 45.1 mm Hg, but this is not consistent in all animals and is largely accounted for by a substantial rise in the single animal, No. 7626. Right ventricular end-diastolic pressure (RVEDP) however, has not risen significantly. Thus, it is clear that left ventricular dysfunction has occurred without right ventricular failure. Systemic blood flow has fallen from an average of 3.32 L/min in the preoperative state to 2.79 L/min postoperatively, representing a decrease of about 15 percent (systemic blood flow does not represent a total left ventricular output, however, since the shunt flow is not included). Table I also contains the hemodynamic data on

TABLE I

Hemodynamic Measurements in Animals with Subclavian Artery-Left Atrial Shunt and Myocardial Infarction

		Early Postoperative Studies						Long Term Follow up Studies				
		LV Pressure		RV Pressure		Systemic Blood Flow						
Dog	Days Postop	Preop mm Hg	Postop mm Hg	Preop mm Hg	Postop mm Hg	Preop l/min	Postop l/min	Fate of Animals	Month	LV Pressure mm Hg	RV Pressure mm Hg	Systemic Blood Flow l/min
6586	8	184/4.8	182/14.0	36.4/4.7	31.5/1.3	3.34	2.57	Died in pulmonary edema 12 days.				
6753	12	142/8.4	171/17.9		43.9/2.9	2.51	2.13	Survived 3½ months.				
6881	8	204/5.1	173/23.6	40.5/0	38.5/5.6	2.64	2.18	Died in pulmonary edema 13 days.				
6922	5	195/6.7	190/23.7	41.9/14.5	49.6/10.6	4.26	4.75	Survived 13 months.	13	247/27	54/4	3.130
7154	14	201/10	183/21.1	43.9/9.4	42.5/8.2	3.91	2.08	Survived 2 months.				
7392	8	124/11.2	144/14.8	38/8.1	37.4/4.7		3.86	Died in pulmonary edema 20 days.				
7626	6	147/8.7	147/22.7	37.6/1.7	53.6/9.2	3.63	2.0	Developed pulmonary edema at 6 weeks, survived 20 months.	20	172/40	59/7.1	3.000
7294	8	122/8.3	146/31	45/2.7	63.8/9.6	3.02		Survived 19 months.	19	168/33	58/7.6	2.170
Average		164.5/7.9	169.5/21.1	40.4/5.9	45.1/6.5	3.32	2.79			199/33	57/6.2	2.73

three of the long-term surviving animals, Nos. 6922, 7626, and 7294, obtained in studies at thirteen, twenty, and nineteen months respectively. These three animals all had patent shunts at the time of study as manifested by persistence of the machinery murmur. Note that the LVEDP has risen further in each case—from 23.7 to 27 mm Hg, from 22.7 to 40 mm Hg, and from 31 to 33 mm Hg respectively. In addition, left ventricular systolic pressure has increased somewhat and right ventricular systolic pressure has increased modestly in two of the three cases, but RVEDP remains at normal levels for these animals. Systemic output in these three animals shows a variable change and remains at the average value obtained for all dogs postoperatively. Thus, even after protracted periods with shunt and infarction, these animals continue to maintain a satisfactory systemic output and ventricular systolic pressure while manifesting further rise in LVEDP. At the same time, even over this protracted period of time, no substantial pulmonary hypertension has developed nor is there any evidence of decompensation of the right heart since RVEDP remains normal.

In order to further study left ventricular function, Table II shows the response of three of the long-term surviving animals to simulated exercise produced by muscle stimulation as compared with results obtained in normal animals. In normal animals, this technique produces a small fall in left ventricular systolic pressure and a small but significant fall in LVEDP. Systemic blood flow is increased by about 55% and there is a 47% increase in stroke volume. Oxygen consumption increases about 300%. By contrast, dogs with left ventricular dysfunction show a distinct increase in LVEDP rising from an average of 18.1 mm Hg to 26.5 mm Hg. Systemic blood flow, which is somewhat lower at rest in the postoperative dogs, rises by about 60% during the exercise period. Stroke volume also increases during exercise in the postoperative animals in a manner similar to that of the normal. Oxygen consumption in the operative animals reveals a 200% increase in oxygen consumption.

TABLE II

Response to Simulated Exercise

(Muscle Stimulation)

	LVSP mm Hg		LVEDP mm Hg		Systemic Blood Flow L/Min.		Stroke Volume		O_2 Consumption	
	Rest	Exercise	Rest	Exercise	Rest	Exercise	Rest	Exercise	Rest	Exercise
Normal*	158	149	8	5	4.20	6.50	26	38	133	525
	Postoperative Animals									
6922	184	147	15.3	24.6	2.39	4.74	10.0	17.2	140	343
7392	144	155	14.4	20.1	3.86	6.21	24.7	36.2	127	478
7626	138	136	24.6	34.9	4.06	5.40	20.3	25.1	167	533

* Average 9 animals.

TABLE III

Response to Ouabain in Postoperative Animals

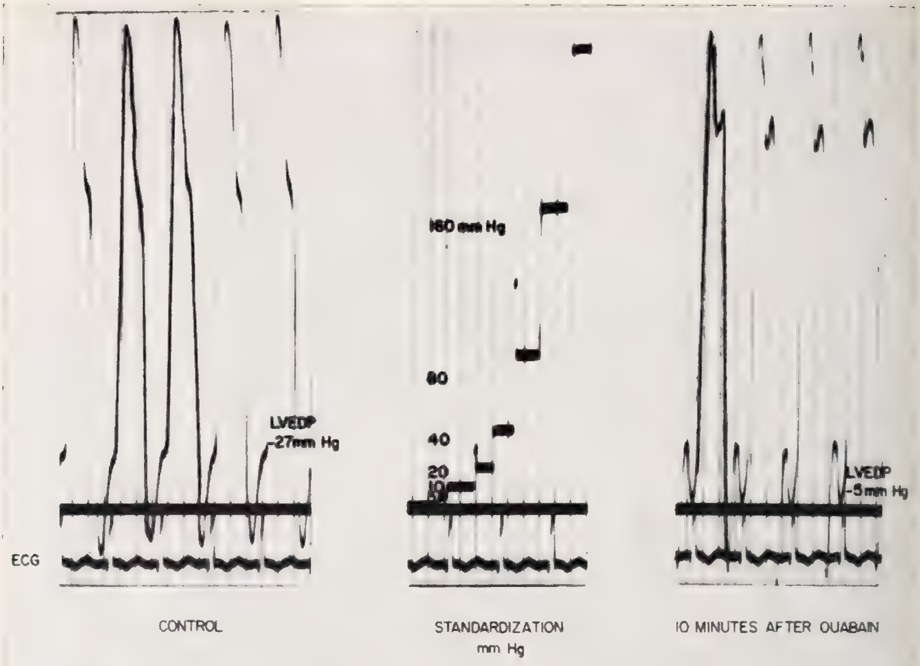
	Dosage	Prior to Ouabain		40 Min Post-Ouabain	
		LV	Systemic Output	LV	Systemic Output
6922	.4 mg	247/27	3.130	176/5.0	3.800
7626	.6 mg	172/40	3.000	200/11.7	3.420
7294	.6 mg	168/33	2.170	136/12.3	3.920

Table III shows the response of three of the long-term surviving animals to digitalis administration (ouabain). Note the very dramatic decline in LVEDP in all animals declining from an average of 33 mm Hg prior to ouabain to 10.7 mm Hg forty minutes following the administration of the digitalis preparation. Systemic pressures have changed variably but remained, on the average, approximately the same. Systemic output which average to 2.73 L min. prior to ouabain administration rose to an average of 3.71 L min. Figure 1 shows one example of the left ventricular pressure response to digitalis administration.

Although no animal developed visible ascites or edema, presence or absence of sodium retention was documented by the periodic determination of total exchangeable Na^{24} space in three chronically surviving animals. Table IV shows a series of measurements made in these three animals at varying intervals as compared with the average of Na^{24} mearurements in normal dogs as found in this laboratory. The normal average value is 6.61 L. All three showed a gradual tendency to decrease in Na^{24} space associated with a modest loss of body weight. In none of the three animals was any tendency to sodium retention noted. Postmortem examination in three animals who died in acute pulmonary edema showed marked left ventricular dilatation with transmural myocardial infarction involving the anterior surface and part of the apex of the left ventricle. In two instances, the myocardial wall in the area of infarction was thin and bulging and appeared to constitute a ventricular aneurysm of about 2 cm in diameter. The base of the anterior papillary muscle was also infarcted in two of the animals. Teflon® grafts were patent throughout. Cut surfaces of the lungs showed edema fluid. Liver, spleen, and kidneys did not show evidence of passive congestion nor was ascites or peripheral edema found. Left ventricular hypertrophy of a considerable degree was noted in all animals.

Discussion

The combination of a shunt between the subclavian artery and left atrium, plus a substantial myocardial infarction in the dog results in clinical and hemodynamic changes which seem to fulfill the necessary criteria for chronic, isolated left heart failure. Thus the animals show cardiomegaly, protracted elevation of LVEDP, reduction in systemic blood flow of about 25 percent, elevation of LVEDP with moderate exercise, marked reduction in LVEDP following ouabain administration, and two to six weeks postoperatively the



RESPONSE OF LEFT VENTRICULAR PRESSURE TO OUABAIN ADMINISTRATION (0.4mg) IN DOG WITH EXPERIMENTAL CHRONIC LEFT HEART FAILURE

Fig. 1. Note the marked decline in LVEDP following ouabain administration in dog with left heart failure, from control value of 27 mm Hg to 5 mm Hg.

TABLE IV

Exchangeable NA^{24} Space in Chronically Surviving Dogs

	Month Postoperative	Na^{24} Space (L)
Normal*	–	6.61
6922	5	6.9
	11	6.5
	12	6.4
7626	1	7.1
	2	7.0
	5	7.0
	8	6.5
	11	6.23
	19	6.27
7294	1	6.91
	8	6.65
	11	6.3

* Average 9 animals.

development of acute pulmonary edema. Ligation of one or two ventricular branches of the left anterior descending coronary artery appears to be sufficient to impair the ability of the left ventricular myocardium to compensate for the volume overload produced by the arterial-atrial shunt.

The average value obtained for exchangeable Na^{24} space as a percentage of body weight, 33.7%, is similar to that obtained by Levitt and Gaudino (5). The value is higher than that found in the adult human.

Until this preparation was reported (1, 2) the only animal preparation showing progressive, chronic left heart failure in significant number was the guinea pig with severe aortic constriction (6). However, it would appear that this preparation is not entirely suited to a study of the hemodynamic and electrolyte disorders of isolated left heart failure since failure of the right heart occurs very soon after operation and the marked aortic constriction necessary to produce failure directly affects renal blood flow because of the reduced flow and pulse pressure distal to the occlusion. An occasional dog with peripheral A-V fistula has been reported to develop pulmonary rales, though only after first exhibiting right heart failure and marked edema (7).

More recently a modification of the current experimental procedure has been reported wherein a diastolic overload shunt from aorta to left atrium was used combined with aortic constriction (8).

The significance of our finding that marked elevation of LVEDP and moderate reduction in systemic output did not result in progressive salt and water retention lies in the contrast between this lack of response and the pronounced retention which can be caused by isolated right heart failure or inferior vena cava ligation (9, 10). We would conclude therefore, that "forward failure" is, in general, not an initiating mechanism in the salt and water retention of most clinical left heart failure and that there are no demonstrable receptors in the left heart and pulmonary venocapillary circulation which are capable of influencing any of the chain of receptors and effectors capable of causing sodium accumulation in the body. Perhaps more profound falls in systemic output or rises in LVEDP might, in themselves, provoke sodium retention but this would be outside of the range of usually observed clinical situations. This work has also demonstrated that acute pulmonary edema may develop due to pump failure of the left ventricle without prior expansion of the body's stores of salt and water. The right heart and venous circulation, however, contain very sensitive mechanisms capable of producing chronic salt and water retention. Despite much experimental work however, there is still a lack of a definitive understanding of the receptor-effector mechanism involved. Recent investigations in dogs with right heart failure do not seem to support the view that a reduction in glomerular filtration rate (GFR) or renal plasma flow (RPF) alone is either necessary or sufficient to promote chronic sodium retention (7), thus turning attention away from alterations in renal hemodynamics as a primary mechanism for salt and water retention. Similarly, the influence of excess sympathetic tone mediated via renal nerves, or the direct influence upon the kidney of elevation in renal venous pressure seem to have been excluded as primary or initiating factors. Excess aldosterone secretion is a constant factor in all animal preparations with chronic heart failure (though not all humans). Aldosterone excess alone will not cause salt and water retention in normal animals or humans, but will do so in the animal with right heart lesions or a ligated thoracic inferior vena cava. Thus a cardiac lesion plus excess aldosterone will reproduce congestive heart failure. In studies of dogs with a large infrarenal aortic-caval fistula, hypersecretion of aldosterone was demonstrated to accompany a moderate reduction in mean pressure and blood flow through the kidney even though cardiac output and renal pulse pressure were increased (7).

In a series of experiments in adrenalectomized dogs, an explanted kidney in the neck was shown to retain sodium when ligation of the inferior vena cava was performed and to undergo sodium diuresis when the ligature was removed (11). These experiments suggested that sodium retention by the kidney was, in fact, mediated by hormonal substances of unknown origin and nature, released in response to stimulation of an unknown receptor mechanism. Therein lies the current state of understanding, leaving open an immense field of future investigation.

Summary and Conclusion

A procedure has been described for the production of chronic left heart failure in dogs. This was accomplished by the additive effect of two lesions—a shunt between the left subclavian artery and left atrium, causing chronic diastolic overloading of the left ventricle and a myocardial infarction produced by ligation of two or more ventricular branches of the left anterior descending coronary artery. Such animals showed a loud to-and-fro machinery murmur, cardiomegaly, and marked chronic elevation of LVEDP, reduction in systemic blood flow of about 25 percent, abnormal rise in LVEDP with exercise, and reduction of LVEDP with ouabain administration and development of pulmonary edema in two to six weeks postoperatively. Protracted survival was possible with continued maintenance of elevated LVEDP in those animals who did not develop pulmonary edema. Despite these abnormalities, salt and water retention did not occur, as judged by the absence of ascites or edema and normal values for total exchangeable sodium space. It is concluded that there are no stretch receptors in the left heart or pulmonary venous system which are capable of initiating sodium retention. The value of this experimental model in future research into the receptor-effector mechanisms of congestive heart failure is described.

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The Evolution of Scientific Method in Medicine

K. D. IRANI*

The notion of scientific method is something that emerges somewhat late in the history of human thought. Quite a bit of science had been accumulated before thinkers became self-conscious about the method which they employed to obtain this knowledge. This, I suppose, is true of most human enterprises. The first point historically where we begin to notice some genuine philosophic interest in this area is not in scientific *method* but in scientific *explanation*. The ancient thinkers must have asked this question: "How do we successfully explain?"

Beginning with the Greeks, two distinct notions emerge rather early. The first powerful trend in Greek thought is Pythagorean—nature is comprehended by laws which state the structure of reality. In comprehending the structure, according to the Pythagorean principle, one comprehends every element in it as internally related to everything else, at which point one understands every single element, and, thereby, the whole. He who extracted the ratio of a structure understood, and was therefore rational. Since, to Pythagoras, being rational and being mathematical were identical, the language of structure was mathematics, and the mode of explanation was deduction. From the mathematical formulation of the general structure, the nature of any specific detail can be deduced and thus explained. Although the total Pythagorean doctrine was severely shaken (not in the least due to the discovery of irrational numbers), the structural approach remained a powerful influence in Western thought.

The other approach emerges in Aristotelian thought—nature is understood in terms of functional laws. One cannot understand a thing until one knows why it became what it became—an approach that needs a dynamic concept of transformation. To this end, Aristotle refined the notion of Cause, and declared there were four kinds, of which two are relevant to this discussion—efficient cause and final cause. Efficient cause is the immediate set of events that transforms an acorn into an oak tree, the combination of water, sunlight, and air. The final cause of the transformation is the inherent potentiality of the acorn itself to become an oak tree—the essence which is actualized in its becoming an oak tree, not a maple; and a tree, not a rock.

Although the Aristotelian philosophy has probably had a wider impact on history, the structuralism of the earlier age began to to be reestablished, particularly by the Roman writers and early Scholastic philosophers who envisioned the universe as a totality of structures with each part having its proper location in a schema similar to the biological classification schemas well known to us.

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This series is under the general direction of Dr. A. S. Lyons, Archivist, the Mount Sinai School of Medicine of The City University of New York, N.Y. 10029.

* Professor of Philosophy, The City College of New York, N.Y. 10031.

This mode of thought led biologists to spend a great deal of time classifying flora and fauna in an attempt to comprehend biological reality in its logical existence. Interestingly, the classification schemes of biology refined by Aristotle were ideologically akin to structuralism, and the classificatory "trees" of biology became the paradigm for all science throughout the Middle Ages.

The ramifications of the structural approach from biology to medicine are interesting to consider. Classifying each entity tends to give the ideal of that type. The science of medicine from the biological perspective attempts to understand the ideal structure of the human body, i.e., the proper relations of ideally defined organs constituting the body. But the physician deals most often with a body that falls short of the classificatory prototype. To the extent that a human body is sick, it has moved away from its proper place in the cosmic order and become a manifestation of a degree of chaos. In death, the decomposing body is in total chaos.

Obviously, this theoretical conception of medical science provides no rationale for systematic therapeutic endeavors. Therapeusis at this time consisted of pure empirical rules without a theoretical base. Meanwhile a quasi-physiological theory provided a basis for medicine in the theory of humors—an outgrowth of the belief that all matter was composed of four elements, viz. fire, earth, air, and water. The four humors of blood, bile, choler, and phlegm combined in certain appropriate proportions to maintain the body in a state of health. An imbalance in the combination caused disease.

Now a therapeutic procedure became possible: improve the balance of humors. Of the two alternatives of supplying a deficit and reducing an excess, the latter was much easier. The prescribed way was bloodletting or bleeding, and the early texts describe bleeding in great detail, much attention given to the location, length, and depth of the cut, and the duration of the letting. Some of these procedures were even employed in the Greek institutions dedicated to Aesculapius, the Greek god of healing. By and large, the "patients" were given rest before and after bleeding, and sometimes given dream analysis and psychotherapy in the bargain.

The conception of humors incorporated a very crude notion of scientific explanation and techniques for therapy, and could not offer adequate explanations when people began to ask methodological questions, such as: What are the efficient causes? How do certain parts of the body affect other parts of the body to maintain the necessary balance?

During the Alexandrian period a new idea came in to supplant the fading theory of humors. An offshoot of the philosophy of the Stoics was the belief in the Pneuma or life spirit which enters matter and brings it to life. The Pneuma ultimately led to a physiological theory of three spirits—natural spirit, animal spirit, and vital spirit. The theory of the movement of these spirits generated a series of problems. For example, the vital spirit was required to go through the heart along with the blood, from left to right, creating a difficulty for medicine, that of explaining how the blood gets from the right to the left side of the heart. Galen thought that there would be tiny holes in the septum, and stretched the septa of the hearts of hogs and other animals, but found no holes. In the Middle Ages, enterprising theologians used this enigma to prove the greatness of God.

From the modern point of view, we would wonder that people in those days—there were some extremely astute thinkers who were subtle in argument, mathematics, geometry, and logic—did not object to this totally unacceptable anatomical and physiological theory. The theory of a vital spirit died partly through the efforts of Servetus, a mathematician, theologian, and part-time anatomist, not quite trained in medicine. Servetus performed demonstrations in anatomy in Paris, and from contemporary reports, it is said that he was considered to be a superb anatomist. Vesalius knew him in Paris and had observed some of his dissections. An early unitarian, Servetus was disinclined to accept the multiplicity of pneumas. He felt that God worked economically, and therefore there was only one spirit which moved everything. It was this view which was to reach fruition in the work of Harvey.

It is difficult to trace Servetus' material because his books were burned with him at the stake by the Calvinists in Geneva. But Harvey mentions that Vesalius supported such a view. This was a period of great ferment in medical science and although Galen was still the established authority the principles of anatomy and physiology were about to change. Knowledge of anatomy became extremely accurate in Padua under the great masters of anatomy, and this work was indeed known to Harvey. But it was in the new physiology that the three spirits disappeared, not because he proved that there was one spirit, but because Harvey established the circulation of blood.

The underlying assumption in Harvey's thinking is a conception of causal continuity. Essentially, one does not explain why something occurs until one can identify the full process which brings it into being and the full process by which it finally disappears. Thus we come to the notion of a process law. This is not just a statement of two events, one event occurring as the result of the other. For instance, X drank poison and a few minutes later X died. Instead of crudely describing the event, science gradually learned to describe the process as a series of events each causing the following one, the last of which is death of X. When the full process is described, the event in question is explained.

Science began to have a change in outlook. Physicians in scientific medicine looked not merely for some connection between events (when A happens, B happens) but for a whole collection of interacting processes in the physiological system.

The starting point of process description in the history of science did not, however, begin with Harvey. The process description had been coming from other sources. As a matter of fact, it was dominant in the physics of Galileo. Instead of explaining the movements of bodies in terms of heavy bodies with a potentiality for going down and light bodies with a potentiality of going up, which was the old description, Galileo offered a very different conceptual description. A satisfactory description is one which gives the change in the position of a body with respect to time. This view is the ideal form of a process description, i.e., a causal description, but by being expressed as an equation it also approximates the old Pythagorean view, in which the mathematical form ultimately explains everything. The distinction between structual and functional explanations which thinkers traditionally were wont to make gradually disappeared when the two became fused.

Fortunately for medicine, the structural-functional debate stayed within the province of the philosophers and did not greatly influence medical practictioners. The great advances in medicine began coming from the military surgeons who had developed interesting techniques for handling broken bones and were making astute observations on the nature of wounds. Medicine began to accumulate a vast amount of empirical data. From this emerged the attempt to explain physical changes in the body in physical terms. The laws of physics and chemistry should be applicable to the body so that certain states, physical and chemical, if appropriately defined, enable one to explain future transformations in those states of the body.

During this period of great advances in some areas of medicine, the great Materialist philosophers of the Enlightenment often used medicine as the foundation for their belief that science and reason would eventually explain the physical world. But even as this view was being put forward, it was charged with being fundamentally inadequate as a total explanation of man and man's place in the scheme of the universe: Where is the conscious agent, particularly the morally responsible agent? How can a machine be charged with praise or blame? Where does a soul fit in; there must be something more than a physical-chemical explanation to explain man?

Some philosophers who pondered these questions were known as the Soul Searchers. There were anatomists who carved up cadavers looking for some appropriate place for the soul. Descartes, one of the pioneers on the subject, said that there was a nonmaterial mind residing in the body. To explain the meeting of the two entirely different forms of reality—mind and body—he claimed that the contact took place in the pineal gland, which seemed to perform no other function. However, people were rather dissatisfied with this gland, and looked for other places for the soul to reside. Many bizarre experiments were performed in the course of the search. Some enterprising researchers placed moribund people in boxes and increased the air pressure in an effort to prevent the soul from leaving the body.

An entirely different field of endeavor, microbiology, provided ideas on the issue of a purely Materialist explanation of living systems. Pasteur's discoveries in microbiology confronted and disproved the theory of spontaneous generation and resulted in the acceptance of the germ theory of disease. The anti-Materialist thesis implicit in this view was that there is no physico-chemical combination which will cause a physico-chemical system at one point to become a living system at the next point. Some nonmaterial living force is required. Pasteur demonstrated this by performing experiments on boiled, life-free sugar solutions that he kept indefinitely free from any living microorganisms by means of hot air passed through appropriately sterilized filters.

It was thus argued that the vital factor was distinct from mechanical factors. The great problem of nineteenth century thought with respect to medicine and biology became how to combine the two. The physicians avoided this dispute because by that time they had become sufficiently oriented to therapy, but, of course, the theoretical biologists still had to confront the problem. Theoretical physicians and biologists were split into two groups, the Vitalists and the Mechanists. They had yet to learn that there was no inherent contradiction between the two views.

The dispute centers on modes of explanation of changes in a biological system. Some changes are goal-directed and some are non-goal-directed. In principle, the non-goal-directed changes can be explained entirely by physics and chemistry. But, according to the Vitalists, goal-directed changes imply some spirit, vital factor, elan vital, or 'entelechy,' the Aristotelian term used by Hans Driesch. Sometimes it was called the life spirit or life spark. On the other hand, the mechanists believed that further discoveries in physics and chemistry would provide proof that goal-directed changes were ultimately purely complex mechanical changes.

In recent years, through the notion of feedback, the problem has come into focus. The concept of feedback, mathematically called cybernetic theory, has clarified the difficulties. It enables us to remove the radical distinction between the vital or goal-directed functions and the nongoal-directed by stating that the goal-directed functions are not inconsistent with a purely physico-chemical causal process. A full discussion of the cybernetic theory and its implications for a synthesis of the two views can be found in the book *Analytical Biology* by G. Sommerhoff.

The application of feedback analysis to goal-directed biological systems is now being actively pursued. For instance, how does a wounded sea animal regenerating a new tail know when to stop the growth of the new tail at precisely the right point? It takes molecular biology to provide the full physico-chemical explanation, as in the work of Jacob and Monod, of the extraordinary and intricate applications of the shut-off mechanism in cellular function. Chemical kinetics explains the reactions of the enzymes at work in the feedback mechanisms. The theoretical problem of explaining goal-directed changes in physico-chemical terms may now be considered to be solved.

We may now examine the notion of Scientific Method itself. Let us briefly reconstruct the method and then indicate the new problems on the horizon which are not yet solved.

The stages of a scientific inquiry are the following: We begin with a problem, i.e., Why does something happen? Next an appropriate hypothesis is constructed. The next stage is the elaboration of the hypothesis, or, in other words, the enumeration of the observable conditions which must exist for the hypothesis to be verified. Observation or experimentation is the next stage. (In observation, there is no attempt to manipulate the values of the observable variables; in experimentation, the values are varied systematically.) The final stage is confirmation or confutation of the hypothesis—confirmation occurring when the elaborated conditions are borne out by repeated observation.

Think of the process of diagnosis. The patient goes to the doctor with a set of symptoms. The problem is to discover the cause of the ailment. Some hypotheses are immediately set up; from past experience the doctor knows that the man could be suffering from several possible maladies. Each one of the hypotheses must be elaborated; that is, the possible observable consequences (i.e., test conditions) of each hypothesis must be stated. We can then determine which hypothesis is true by finding out which of the test conditions were satisfied in observation.

Not all scientific inquiry is of the diagnostic kind. We may have a research inquiry. The difference between a diagnostic and a research inquiry is that whereas in the former the investigator has a pregiven list of hypotheses from which it is his task to select the right one, in the latter the investigator must invent one or more suitable hypotheses. The crucial part of research is the invention of hypotheses. The question now is: Given a problem, how does one invent hypotheses? There is no reliable methodology for constructing original hypotheses. If there were, scientific research could be left entirely to a computer.

When a researcher constructs a new hypothesis he employs some general concepts, which, on some general grounds, are believed to be workable. This is called the Conceptual Framework of the science at the time.

What the development of scientific method shows is that two things have changed: one, the kind of law that is considered as providing a good explanation; and two, the kinds of concepts that go into the formulation of hypotheses. We may consider both of these separately.

We saw the development from the structural and Aristotelian notions through physiological process descriptions to present-day physico-chemical feedback process descriptions which seem to be adequate for the problems that we face today. And with regard to the development in the concepts we employ in our laws we saw the change from early potentiality concepts through the humors, the pneumas, into present-day germ theory and the chemical theory of toxins that emerges from it.

I will now raise one problem which at the moment seems rather difficult to handle, that is, the problem of relating biology to psychology: What physico-chemical description of the nervous system is adequate to explain behavior? Behavior unfortunately is not a unitary notion. You could be a strict behaviorist, in which case you take the organism, subject it to controlled stimuli, and observe the responses. That would be the old fashioned stimulus-response scheme. Or you could be a Skinnerian and use the notion of operant conditioning.

What this omits is the description of the individual when he thinks. This is given in nonbehavioral terms, if you like, ordinary language, but then you can also be a behaviorist and treat language as behavior. That is not altogether satisfying, because when I say for example that I feel something or that I think something, I am not just behaving by uttering some words. I am also, at least as far as I am concerned, believing that I am referring to something in my mind. Now what do we do? We give another description. This is the nonbehavioral description.

We have two completely different descriptions of behavior: one, the behavioristic, given in terms of movements or changes of the organism in space and time; the other, what is called the phenomenological description—that is, a description of states of consciousness in terms of beliefs, wants, inclinations, intentions, decisions, and so on. We have to relate these two to each other and to neurological descriptions.

Where is the conceptual scheme which enables us to do this? We don't have one. But it is very much worth going into. I have talked with a few neurologists who have been less than enthusiastic about this. I have talked to behaviorists who have not been enthusiastic about phenomenological descriptions and I have talked to phenomenologists who have not been enthusiastic about behavioral descriptions, nor about neurological ones.

Regarding phenomenological descriptions one may be inclined to say, let's get rid of introspective psychology. I don't think we can do it. But more interestingly, phenomenological concepts are the concepts which are used in psychoanalytic descriptions. In psychoanalysis, one uses phenomenological terms like wants, beliefs, motives, intentions, with the added complication of making them unconscious. But the logic of this can be worked out. Not enough has been done. Sooner or later science will call upon its practitioners to provide a new conceptual framework. That would constitute a further development in the conceptual structure of science.

Granular Cell Myoblastoma of the Extrahepatic Biliary Tract

ARTHUR B. ABT, M.D., EDWARD FEINBERG, M.D., AND SAUL KUNITZ, M.D.

Introduction

Granular cell myoblastoma is an uncommon benign tumor first described in 1926 by Abrikossoff (1). In 1952, the first case of granular cell myoblastoma of the extrahepatic biliary tree was reported by Coggins (2). Since that time seven more cases of biliary tract myoblastomas have been reported (3–8). The purposes of this communication are to present the clinical and pathologic findings of an additional case, and to compile the available clinical information on the previously reported cases.

Case Report

V.K., a 44-year-old Negro woman was first seen at The Mount Sinai Hospital with intermittent right upper quadrant pain of one week duration. The pain was unrelated to food intake and there was no history of jaundice, dark urine, or light stools.

The patient was well developed, anicteric, and afebrile. Pertinent physical findings were limited to the abdomen and included right upper quadrant tenderness to palpation. No mass was palpated.

Laboratory data including hemoglobin, hematocrit, urinalysis, bilirubin, serum glutamic oxalacetic transaminase, and alkaline phosphatase were all within normal limits. The white blood cell count was elevated to 12,800 with 75% segmented neutrophiles, 5% bands, 19% lymphocytes, and 1% basophiles. Repeated cholecystography failed to visualize the gallbladder. When a laparotomy was performed a solitary tumor mass was noted to obstruct the lumen of the cystic duct just distal to its junction with the common duct. The gallbladder and tumor mass were excised. A frozen section of the tumor was reported as granular cell myoblastoma. Following the operation the patient made an uneventful recovery.

Pathologic Findings

The specimen consisted of the gallbladder and cystic duct. The gallbladder measured 8 × 2 cm and had a thickened wall. It contained a small amount of green bile and several small black irregular calculi. The cystic duct was dilated, fibrotic, and contained multiple black irregular calculi measuring up to 4 mm in diameter. A firm rubbery white nodule with yellow streaks located 1 mm from the resection margin measured 1.0 × 1.0 × 1.2 cm. The nodule appeared to obliterate the lumen of the cystic duct (Fig. 1).

Microscopic examination revealed a tumor composed of clusters of round and

From the Departments of Pathology and of Surgery, Mount Sinai School of Medicine of The City University of New York, New York, N.Y. 10029.

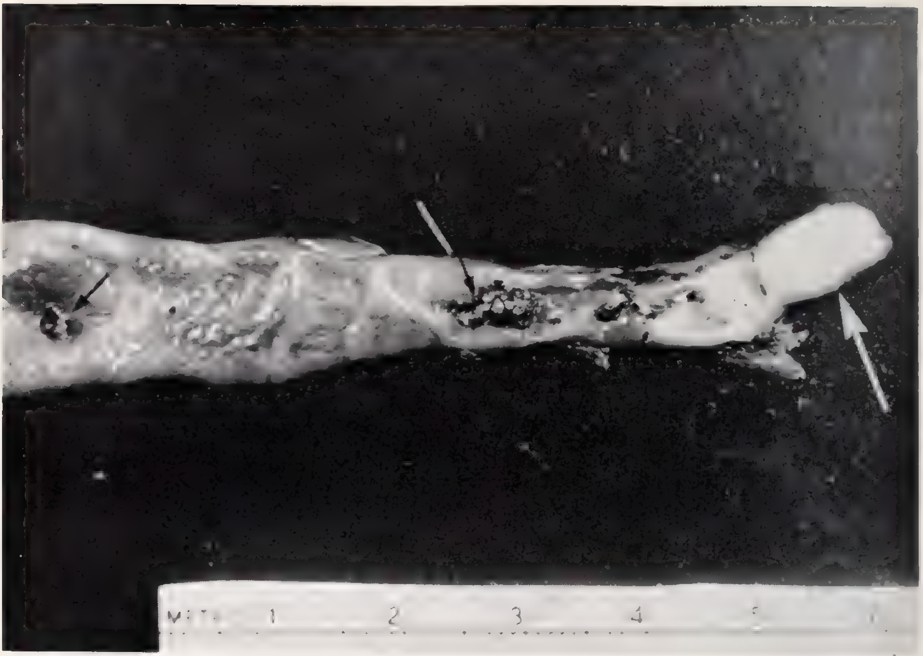

Fig. 1. Gallbladder and cystic duct showing tumor nodule (white arrow) at resection margin and stones in gallbladder and cystic duct (black arrows).

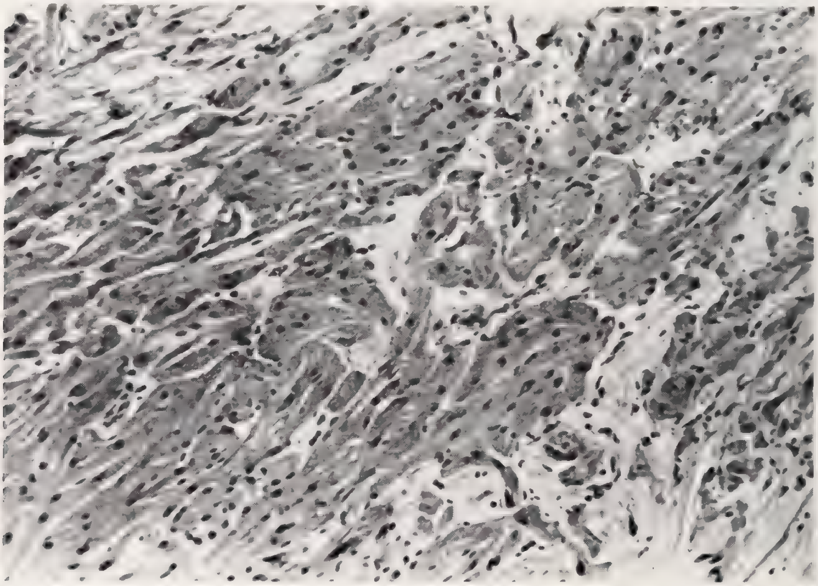

Fig. 2. Clusters of cells with granular cytoplasm and dark staining nuclei are apparent. Light-staining bands of collagenous tissue surround groups of these granular cells. (hematoxylin and eosin × 100).

TABLE I

Summary of Clinical Features of Biliary Tract Granular Cell Myoblastomas

Case	Author	Age	Sex	Race	Symptoms	Duration of Symptoms	Treatment	Result	Comment
					Common Duct				
1	Coggins (2)	25	F	N	Anorexia, vague abdominal complaints, 20 lb. weight loss in 1 month, jaundice	1 year	None	Death from hepatic failure	Arrived at hospital moribund
2	Duncan (4)	30	F	N	Progressive jaundice	1 month	Excision and cholecystectomy	Uneventful recovery	Tumor at hepatocystocholedochal junction
3	Whitmore (7)	37	F	N	Painless jaundice with 1 week light stools, dark urine	1 week	Excision and cholecystectomy	Uneventful recovery	
4	Whitmore (7)	61	F	N	None				Incidental finding at autopsy
					Cystic Duct				
5	Serpe (5)	34	F	N	Right epigastric pain, nonvisualization of gallbladder	9 months	Excision and cholecystectomy	Uneventful recovery	
6	Goldman (6)	14	F	N	Right upper quadrant pain, nonvisualization of gallbladder	1 month	Excision and cholecystectomy	Not mentioned	Gallstones were present
7	Fialho (3)	21	F	N	Intermittent colicky pain	5 years	Excision and cholecystectomy	Uneventful recovery	
8	Christensen (8)	34	F	W	Epigastric pain	1 year	Excision and cholecystectomy	Not mentioned	Patient had hydropic gallbaldder
9	Abt	44	F	N	Right upper quadrant pain, nonvisualization of gallbladder	1 week	Excision and cholecystectomy	Uneventful recovery	Gallstones were present

elongated cells with granular eosinophilic cytoplasm and indistinct cytoplasmic borders. The nuclei were frequently small and stained darkly with hematoxylin; a few were large and vesicular (Fig. 2). The granular cell clusters were separated by bands of pink-staining collagenous tissue. Portions of cystic duct mucosa surrounded by fibrous tissue were identified within the tumor. Nerve fibers were seen at the periphery of the tumor mass. The pathologic diagnosis was granular cell myoblastoma.

Discussion

Benign tumors of the biliary ducts are uncommon and granular cell myoblastoma in this location is rare (9). The reported cases of biliary tract myoblastomas may be divided into two groups (Table I). The first includes those resulting in common duct obstruction and symptoms of painless jaundice. The only reported fatality was caused by a tumor in this location. The second group consists of those involving the cystic duct and causing symptoms of right upper quadrant pain unaccompanied by jaundice. Two of these patients had cholelithiasis which has been suggested as being secondary to the obstructing tumor (6). In no case was the proper diagnosis made until a laparotomy was performed.

A review of the reported cases (Table I) shows that all nine patients were females and that eight of the nine were Negro. A recent series of granular cell myoblastomas occurring in diverse anatomic locations revealed a female to male ratio of 2:1 and a Caucasian to Negro ratio 9.5:1 (10). Another series also showed these tumors to be more prevalent in females, but 74% of these patients were noted to be Negro (11). While the number of patients with biliary tract granular cell myoblastomas is small, there is no apparent reason for the exclusive occurrence in females or the marked predominance in Negroes.

Granular cell myoblastoma of the extrahepatic biliary ducts is an uncommon but curable lesion. It should be considered in the differential diagnosis of extrahepatic biliary obstruction or cholecystitis.

Summary

A patient with granular cell myoblastoma involving the cystic duct is presented. The clinical features of eight previous cases of biliary tract myoblastoma are reviewed. In three of the four cases involving the common bile duct, symptoms of extrahepatic biliary obstruction were present and all five cases occurring in the cystic duct had symptoms compatible with chronic cholecystitis. All patients were female, and all but one were Negro.

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A New Device for the Restoration of Partially Amputated Hands

FRANCES DWORECKA, M.D., LAWRENCE H. WISHAM, M.D.,
AND RICHARD SMITH, M.D.

We are reporting a technique for making a prosthesis which provides for the retention of sensation in a partially amputated hand and permits the functional use of the hand in two-handed activities while at the same time allowing for fairly good cosmesis. Sensory function is often overlooked in the rehabilitation of the patient with a partially amputated hand. The ability to feel an object while holding it, and knowing the position of the hand without looking at it are necessary components of normal hand function. It has been a common practice to provide patients with partially amputated hands with cosmetic gloves which give a reasonably good appearance of a normal hand. Such gloves, however, do not permit sensation and, consequently, are not optimally functional. Another common practice has been to provide the patient with a mechanical grasping device (most often the "Robins Aid"). This device gives a strong mechanical grip, but the lack of sensation prevents good functional use. A third method in the treatment of these patients has been ablation of the hand and replacement with a prosthesis. This too leaves the patient with a hand lacking sensation.

Our approach to the partial hand amputee is concerned first with restoration of function and secondarily with cosmesis.

Method

Initial evaluation includes a careful medical and vocational history. An outline of the partially amputated hand is made and palm prints are taken. Measurements of the active and passive range of motion of the wrist and remaining joints of the hand are made. X-ray films of the hand are taken to determine the integrity of the remaining bones. Testing of prehensile strength, of the ability to manipulate fine objects, of activities of daily living, and of motions involved in vocational activities are performed.

The result of the examination determines the indications for reconstructive surgery, some form of prosthesis, or a combination of both. It is usually necessary to fabricate a device which will simulate the permanent prosthesis or, as in a case of planned surgical correction, will position the digit to simulate the final result of corrective surgery.

If a device is to be fabricated, a negative mold of the partially amputated hand is made and then a postive is made of plaster of Paris. Devices are then fashioned with prenyl or isoprene. Prenyl of $\frac{1}{16}''$ thickness is used. This material is easily molded after heating to 140°F and it sets in twenty minutes. Velcro fastenings are glued or riveted to the device. The following case summaries illustrate the method.

From the Department of Rehabilitation Medicine, The Mount Sinai Hospital, New York, N.Y. 10029.

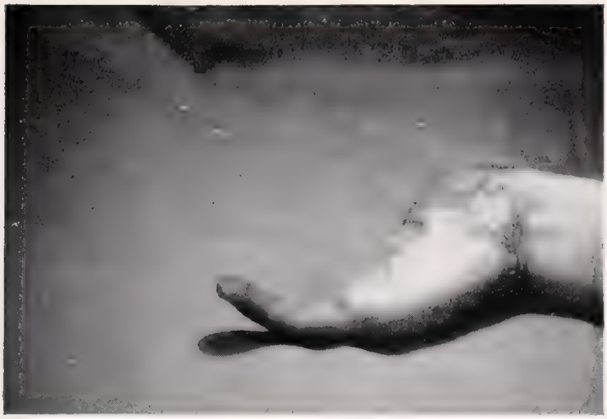


FIG. 1. Right little finger osteotomy and rotation.

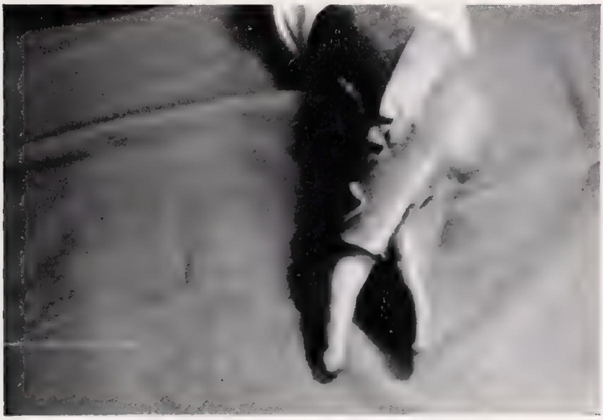


FIG. 2. A prenyl stationary post.

Case 1: A 28-year-old male mechanic was considered as a radial hemiamputation. The patient had only a right little finger. In order to provide the patient with a more functional stump, the little finger was osteotomized and rotated so that opposition against a post was possible (Fig. 1). A prenyl stationary post was made and placed on the hand stump to permit maximal range of motion of the finger (maximal range is one inch) (Fig. 2). Maximal pinch force was one pound. The patient was able to pick up pegs ranging in size from $\frac{1}{16}$ of a inch to $1\frac{1}{2}$ inches. He was able to write, and to assist the remaining left hand in two-handed activities such as tying shoe laces. When he first used the device, he could not manipulate objects and he lacked force sufficient for holding most objects related to his interests and his occupation as a mechanic. Three months following application of the splint, the patient was able to pick up and hold with the device small objects such as coins, paper clips, match boxes, and other objects less than one inch in diameter with very good sensibility and surprisingly strong power.

Case 2: A 19-year-old male college student was considered as an ulnar

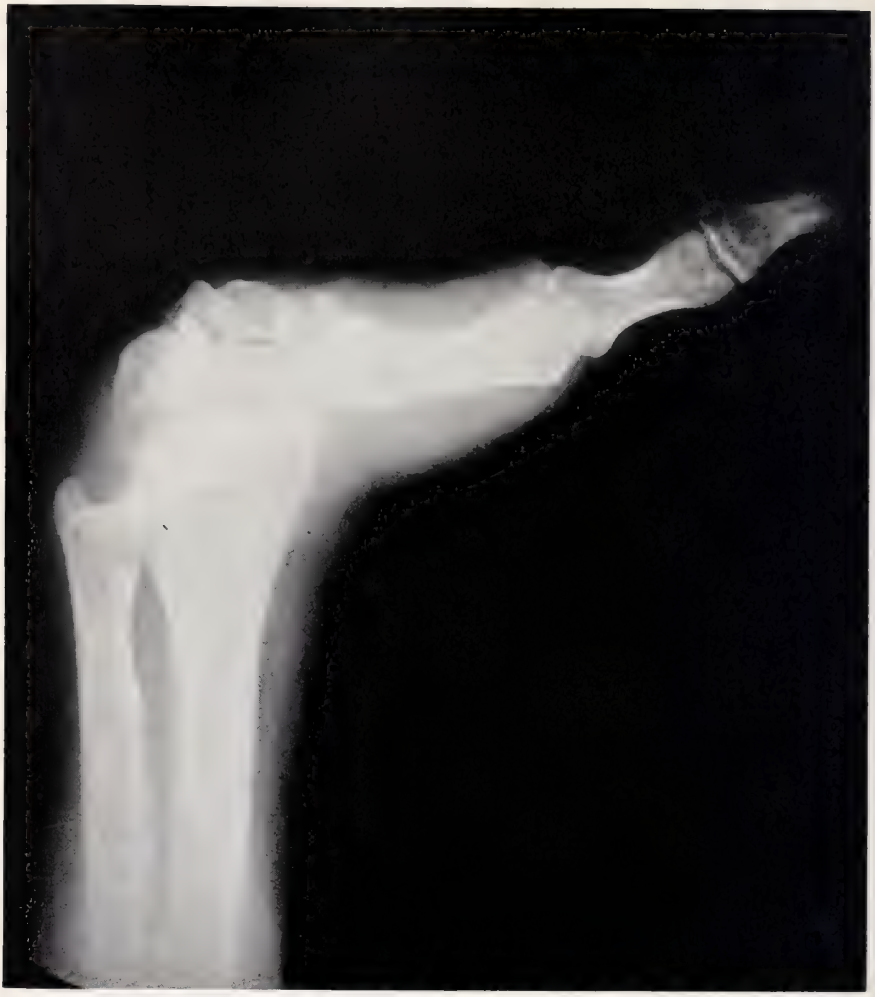
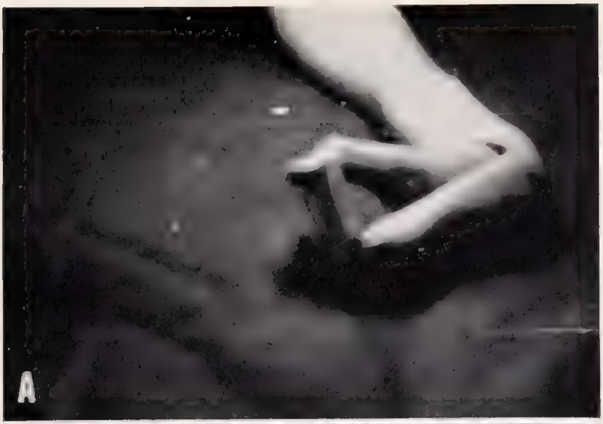


Fig. 3. Case 2. Because of muscle imbalance the thumb is in a position of hyperextension and hyperabduction.

hemiamputation. The patient was left with a thumb, the rest of the hand having been amputated as a result of surgery for a tumor (Fig. 3). The patient carried the thumb in a position of hyperextension and hyperabduction; active wrist extension was limited to 20° with good motor power, active wrist flexion was 30° with normal strength. The carpometacarpal joint was unstable. The metacarpophalangeal joint showed normal range but active motion was impaired. The function of the interphalangeal joint was within normal limits. The patient used the thumb in the hyperabducted position as a hook for carrying light objects. A device was constructed consisting of an opposition post against which pinch could be achieved (Fig. 4a). The first two such devices failed to provide useful prehension because of the unstable carpometacarpal joint. A third device was constructed which consisted of two parts—a splint stabilizing



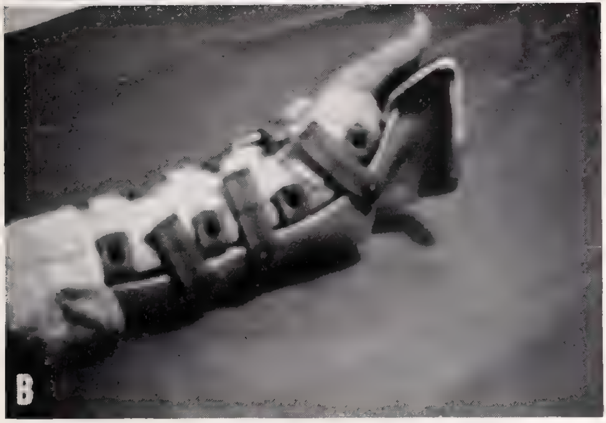


Fig. 4a. The initial splint used in the evaluation of case 2.
Fig. 4b. The temporary splint used for evaluation for possible surgical correction.

the wrist, carpometacarpal joint, and metacarpophalangeal joint; and an opposition post fitted over the splint (Fig. 4b). This device was successful in providing good prehension. He was able to pinch with a force of 9 lbs and was able to perform a wide variety of two-handed activities such as removing and lighting a paper match, tearing paper, holding a nail with the involved hand while hammering with the right hand. The evaluation completed, the problem was discussed with the surgeon. It was decided to stabilize the carpometacarpal joint with a Kirshner wire and to transfer the brachioradialis muscle to the proximal phalanx of the thumb, using the palmaris longus as a tendon graft at the same time. This resulted in a stable carpometacarpal joint and more useful flexion power. The patient was then able to use the digit against the device. Finally, we provided the patient with a cosmetic hand which included a post against which he was able to achieve the same degree of pinch power as he could with the splint (Fig. 5).

Case 3: A 17-year-old male was considered a distal hemiamputation. The patient was left with only the metacarpal and a short stump of the proximal

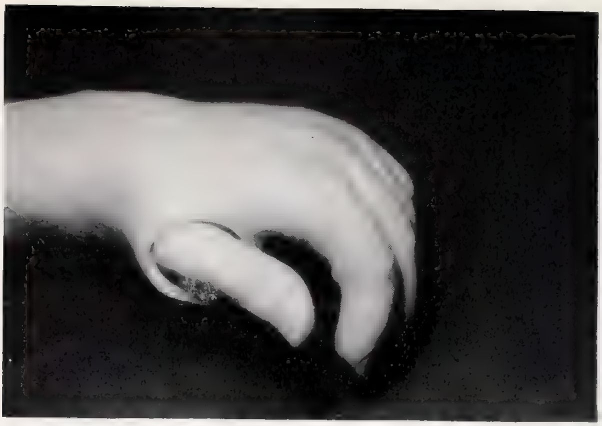


Fig. 5. Partial hand prosthesis used in case 2.

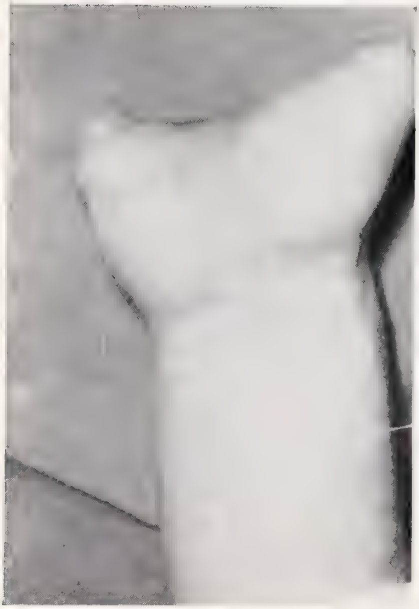


Fig. 6. Case 3 prior to surgical elongation of the stump of the thumb.

phalanx of the right thumb, all other phalanges and metacarpals were amputated following an accident at work (Fig. 6). At the time of the initial evaluation, the patient had normal function of the wrist and good thenar function which was of little or no value because of the short thumb stump. He was provided with a stocking-type prosthesis which increased the length of the thumb by ⅜ of a inch and with a partial hand splint (Fig. 7). With these devices he was able to hold objects of up to ¾ inch in diameteer and as fine as a pin. He was able to use a screwdriver and scissors with the involved hand. We then recommended increasing the length of the thumb surgically. This was done using a bone graft from the ilium and rotating a skin flap to cover the new bone (Fig. 8). Following successful surgery, he was provided with a partial hand

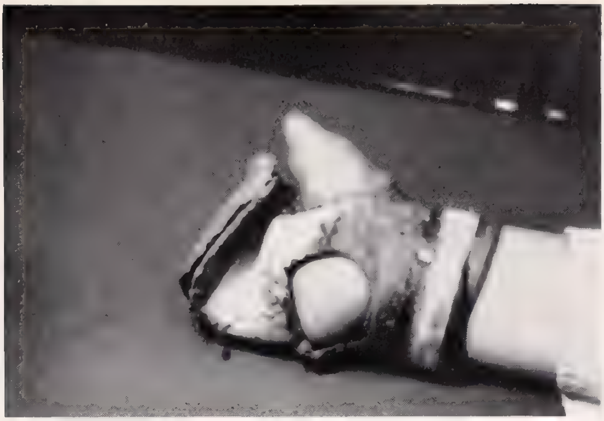


FIG. 7. The partial hand splint used in case 3.

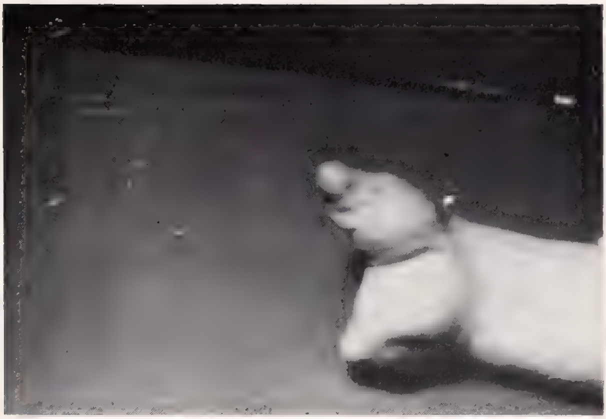


FIG. 8. The stump after surgical correction.

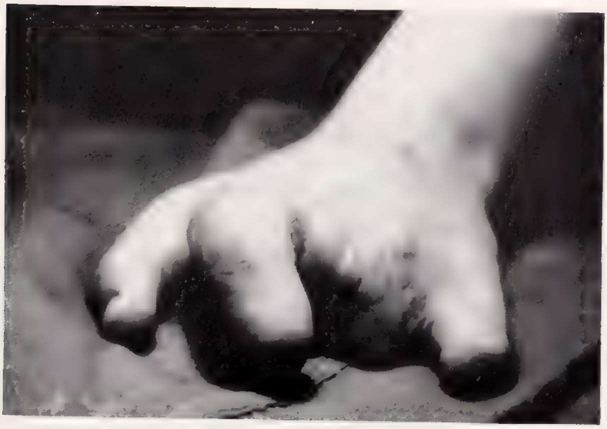


FIG. 9. Ulnar deviation of the index finger in case 4.

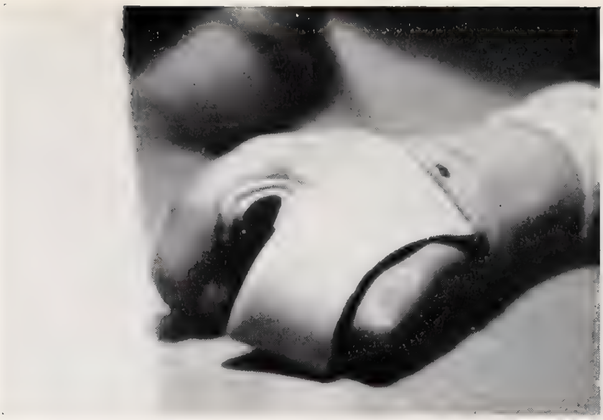


FIG. 10. Functional splint used in case 4, for stabilization of the M-P joint of the index finger.

splint, a cosmetic hand, and a Robins Aid device. The patient now attends a technical school and is interested in drafting which he is able to do using the hand splint. He prefers the hand splint to the cosmetic glove and the Robins Aid, and wears it almost constantly.

Case 4: A 14-year-old male was considered as an ulnar hemiamputation. The patient was left with a thumb, index finger, a part of the proximal phalanx of the long finger and a little finger. The thumb function was normal; there was instability and subluxation of the metacarpophalangeal joint of the index finger, the proximal interphalangeal joint of this finger was fused at 45° on flexion, the distal interphalangeal joint had an active range of motion from 55° to 90°. The little finger showed normal motion at the metacarpophalangeal joint; the interphalangeal joints were fused (Fig. 9). The patient was fully capable of tip pinch, but had difficulty with lateral pinch because of instability of the index finger which lacked the support of the missing fingers. This resulted in loss of strength in lateral pinch. A splint was made to substitute for the missing middle and ring fingers, curved and shorter than normal so as not to interfere with prehension between the thumb and little finger (Fig. 10). The splint aids the patient in his performance using a heavy tool; in all other respects the patient performs as well or better without the splint, particularly in fine manipulative motion. In this case, the patient wears his splint only when he needs it for grasp of heavy objects.

Conclusion

A method of evaluation and prosthetic replacement of a partially amputated hand is discussed. It is simple, practical, and inexpensive, and is well accepted by our patients, all of whom feel that any device that permits sensation is preferable to an insensate device such as a hook or cosmetic glove. Prosthetic replacement described above is functionally superior because it allows the maximum use of the remaining part of the hand. All our patients who were fitted with a Robins Aid and cosmetic glove discarded them as functionally limiting. It is our experience, despite general belief, that the patient does not pay much attention to the texture or color of a device if the gross shape reminds him of a hand and it is functional. Any device that permits sensation is always preferable to an insensate device such as a hook, Robins Aid, or cosmetic glove. The concept of ablation at the wrist of such partially amputated hands has been advanced by many prosthetists and some surgeons. Our experience has indicated that one should always preserve and use whatever is left.

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Peritonitis Due to Salmonella Typhimurium Complicating Nutritional Cirrhosis

SHALOM Z. HIRSCHMAN, M.D. AND SHEILA MURPHY, M.D.

Primary infections due to Salmonella species other than Salmonella typhi, have been described in almost every organ (1–4). The Salmonella organisms are notorious opportunists. Yet peritonitis due to Salmonella species without overt septicemia, appendicitis, or intestinal perforation must be exceedingly rare since this entity has not been featured in the literature.

We report a patient with nutritional cirrhosis who developed peritonitis due to Salmonella typhimurium while being treated for hepatic decompensation.

Case Report

The patient, P.S., a 40-year-old woman from Puerto Rico was admitted to The Mount Sinai Hospital on November 28, 1970 complaining of nausea and vomiting of one month's duration, and of black stools, dark urine, diarrhea, right upper quadrant pain, and abdominal swelling of three weeks' duration. The patient also complained of back pain and dysuria of three weeks' duration, and right pleuritic chest pain without cough or hemoptysis of two weeks' duration. The patient drank two pints of whiskey per day for the past fifteen years. The medical history revealed attacks of pyelonephritis, 9 years, 3 years, and 1 year before admission, all treated with sulfisoxazole. In 1953 the patient was treated with penicillin for gonorrhea; and she claimed that she had malaria with jaundice at the age of 11 years. Her mother had diabetes mellitus and filariasis. The physical examination on admission showed a rectal temperature of 102°F, a pulse of 104, a blood pressure of 110/40, and a weight of 140 pounds. The patient was a jaundiced and lethargic woman. Examination of the skin showed arachnoid nevi on the chest and palmar erythema. There was a fresh hemorrhage in the right retina. The right diaphragm was elevated but the lungs were clear to auscultation. A grade 2/6 systolic ejection-type murmur was heard along the left sternal border between the second and third intercostal spaces. Abdominal examination revealed ascites with shifting dullness. The liver edge was palpable five fingerbreadths below the right costal margin but the spleen was not palpable. There was bilateral costovertebral angle tenderness, greater on the left than on the right. There was slight bilateral pedal edema. The stool hematest was negative. Admission laboratory values were: hemoglobin, 10.9 Gm/100 ml; white blood cell count, 17,600 per mm^3 with 58 mature polymorphonuclear leukocytes, 16 band forms, 2 eosinophils, 17 lymphocytes, and 2 monocytes; blood urea nitrogen (BUN), 5 mg/100 ml; fasting blood glucose, 115 mg/100 ml; bilirubin, 9.8 mg/100 ml with 7.7 mg direct reacting; alkaline phosphatase, 195 international units; lactic dehydrogenase (LDH), 190 inter-

From the Division of Infectious Diseases, Department of Medicine, Mount Sinai School of Medicine of The City University of New York, N.Y. 10029.

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national units; serum glutamic oxaloacetic transaminase (SGOT), 150 international units; erythrocyte sedimentation rate (ESR), 100 mm/hr (Westergren); PBI, 5.5 gamma per 100 ml; and prothrombin time 20.8 seconds (control of 12.4 seconds). The urinalysis showed a specific gravity of 1.004; 4+ bile; urobilinogen, 1:80; and 15–20 white blood cells per high power field. An intermediate strength PPD skin test was negative. Serum protein electrophoresis showed diffuse increase in the gamma G globulin fraction and the agar immunodiffusion test for Australia antigen was negative.

The urine culture showed one million colonies of Klebsiella species per ml and the patient was begun on cephalothin, 6 gm per day, two days after admission. A paracentesis on November 30, 1970 yielded a slightly cloudy yellow ascitic fluid with a specific gravity of 1.012 and a white blood cell count of 298 per mm^3, mainly mononuclear cells. The bilirubin concentration of the ascitic fluid was 1.4 mg/100 ml and the protein concentration 1.2 Gm/100 ml. Culture of the ascitic fluid yielded no organisms.

On December 3, 1970, the patient had a rectal temperature of 105°F. Paracentesis was repeated and the patient was begun on gentamicin therapy. Elevations of rectal temperatures to 100.8°F continued, and on December 7, 1970 diarrhea developed. An intravenous pyelogram was normal. Paracentesis was repeated on December 9, 1970. The ascitic fluid had a protein concentration of 1.5 Gm/100 ml; a glucose concentration of 56 mg/100 ml; a white blood cell count of 23,900 per mm^3 with 90% neutrophils; and a red blood cell count of 1660 per mm^3. On December 14, 1970 the culture of the ascitic fluid removed on December 3, 1970 was reported to contain a group B Salmonella. The patient was begun on chloramphenicol therapy and made an uneventful recovery. In the hospital she lost twenty pounds since admission and her abdominal swelling markedly decreased. Stool, blood, and urine cultures were negative for Salmonella. The organism was identified as Salmonella typhimurium at the Center for Disease Control, Atlanta, Georgia.

Discussion

Peritonitis is a recognized complication of nutritional cirrhosis. The organisms most often causing this complication are Escherichia coli and Aerobacter aerogenes (5, 6). Although Salmonellosis has frequently been associated with liver disease, peritonitis per se without other complications such as bacteremia has not been noted. Havens and Wenner (7) described two cases of Salmonella cholerasuis septicemia in 23 human volunteers experimentally infected with the agent of hepatitis. Bennett and Hook (8) suggested that Salmonellosis is more apt to occur in the same poor sanitary conditions that favored the spread of viral hepatitis and that this factor accounted for the frequent association of Salmonellosis and jaundice (9). In an epidemiologic study of Salmonellosis in New York City, Cherubin et al (10) pointed out that S. typhimurium was the most common serotype found in New York City and that it seemed to produce more than its share of severe disease, having been associated especially with serious preexisting diseases. Furthermore only one half of the patients with S.

typhimurium septicemia had positive stool cultures. These authors (11) suggested that S. typhimurium might persist as an intracellular parasite and could be liberated to cause disease when the function of the reticuloendothelial system had been sufficiently impaired by a supervening debilitating disease.

Patients with hepatic cirrhosis are more susceptible to blood stream infection by enteric gram negative bacilli (12, 13), and a number of cases of Salmonella bacteremia complicating chronic liver disease have been described (4, 13). It has been suggested that the colon in patients with cirrhosis is more permeable to transmural migration of bacteria and that this would account for the increased incidence of peritonitis caused by enteric organisms in these patients (5). This mechanism of infection may have been operative in the case presented.

Summary

A patient with hepatic cirrhosis complicated by S. typhimurium peritonitis is presented. Blood, stool, and urine cultures were negative for this organism. The association of hepatic cirrhosis and infection and the mechanisms of infection that may have been operative in this case are discussed.

Acknowledgment

The authors thank the members of the Department of Diagnostic Microbiology of The Mount Sinai Hospital for their assiduous efforts in the isolation and identification of the organism.

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The Problem of Screening in Hypertension

MILTON MENDLOWITZ, M.D.

In most minds the word "epidemic" signifies the spread of a communicable disease, such as influenza or plague. These diseases, however, have been brought under relative control in most civilized nations by sanitation, hygiene, vaccines, antibiotics, etc. The center of the epidemiologic stage, therefore, which used to be occupied by communicable diseases, has been gradually usurped by such diseases as hypertension, arthritis, diabetes, atherosclerosis, and cancer which are often called "degenerative" diseases. This is an unfortunate word which implies that such diseases are a natural degeneration of organic processes which eventuate in disability or death regardless of therapy.

The epidemiologic target is always prevention of disease. In communicable diseases, incidence, distribution, vectors, host-resistance, and other elements are important because it is by attacking these factors that such diseases are prevented. In the so-called degenerative diseases, however, the usual epidemiologic interest in such things as vectors or contacts does not apply with reference to the ultimate goal, namely prevention. What does apply is the study of genetics, diet, social milieu, and similar factors. Most medicine today should be preventive medicine and when really sick patients are "treated" in our offices or hospitals, such patients usually represent failures of prevention. If a diabetic is prevented from accumulating glucose, diabetic ketoacidosis is avoided. If a malignancy is removed in its early stages, metastases are prevented, just as, when poliomyelitis vaccine is administered, the development of that disease is prevented.

The most prevalent cause of death in the civilized world today is arteriosclerosis with its catastrophes of myocardial infarction, stroke, and gangrene. Many factors, both constitutional and environmental, influence this process. All of these factors should be attacked but whether such control decelerates atherosclerosis in all instances is still a moot subject which requires continuing investigation. Among the suspected factors are diet (1), tobacco (2), diabetes (3), gout (4), personality pattern (5), lipid metabolism (6), and hypertension (7). The relative importance of each of these factors, and of others, is still unsettled and the ability to control or modify them is variable and imperfect.

I propose to focus attention on one factor, namely hypertension. It is generally agreed that hypertension accelerates atherosclerosis (8), and that it produces retinopathy, nephrosclerosis and renal failure, and increases the incidence of stroke and coronary arteriosclerosis, with its sequelae of myocardial infarction and congestive heart failure (9, 10). What is more, relatively effective therapy is available for the control of hypertensive disease and such therapy

From the Department of Medicine, Mount Sinai School of Medicine of The City University of New York, N.Y. 10029.

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has been continually improved over the past twenty years (11, 12, 13). The evidence that such treatment decelerates the sequelae of hypertension and hence morbidity (14) and mortality (15, 16) is also becoming more and more convincing, although controlled studies, particularly of early hypertension, are still needed.

It is estimated that at least one in ten people in this country either have or will have high blood pressure (17) and the incidence is greater among certain groups, particularly the urban black population (18). Treatment of hypertension, therefore, represents one of the greatest experiments in preventive medicine ever undertaken.

In its early stages, hypertension is asymptomatic, so that, unless we are to depend on random discovery of elevated blood pressure by a physician during a chance examination, case finding in the field is mandatory, particularly in disadvantaged populations where routine medical examination is uncommon. For such a program to be successful, a team headed by a physician must have the cooperation of an organized community and be able to go into the home, and carry out blood pressure measurements. Automatic objective devices which can be used by paramedical personnel are available for such purposes (19).

Once people with elevated blood pressures are identified, an elaborate back-up organization must come into play. Some of these subjects will have transient elevation of blood pressure due to anxiety alone (20). Some will have renovascular disease (21, 22). Others will have chronic renal parenchymal disease such as glomerulonephritis and still others will have such adrenal diseases, as pheochromocytoma (23), Cushing's syndrome (24) and primary aldosteronism (25). The bulk of these subjects, however, will have hereditary essential hypertension. The sifting out of these conditions, which can, not infrequently, coexist in the same subject, requires medical work-up together with supplemental testing.

Each hypertensive subject must first have a routine medical examination, consisting of history, physical examination and such laboratory tests as urinalysis, complete blood count, erythrocyte sedimentation rate, electrocardiogram, chest x-ray, and an automated blood chemistry survey including serum sodium, potassium, chloride, carbon dioxide, calcium, phosphorus, uric acid, lipid profile, and fasting blood glucose and blood urea nitrogen. If indicated, total serum proteins and protein electrophoresis can be added. This will usually serve to weed out cases of chronic nephritis, diabetic renal vasculitis, gout, etc. In addition, each patient should have a rapid sequence intravenous pyelogram (IVP) (26) and a routine catecholamine metabolite (CM) test for pheochromocytoma (27). In our clinic, we would also screen for hereditary essential hypertension by means of a tritiated norepinephrine uptake (TNEU) test (28).

If the patient has hereditary essential hypertension, the last test will be positive and all the others negative and treatment can be begun. Eighty percent or more of the patients will fall into this group.

A positive test for pheochromocytoma, confirmed by several additional urinary tests will direct therapy toward the goal of surgical removal of the tumor.

If the TNEU tests and the CM tests are negative, however, much more elaborate testing will be necessary. The negative TNEU test will have to be confirmed by a normal digital vascular reactivity (DVR) test (29) and normal apparent norepinephrine secretion rate (ANESR) test (30). Such reinforcement is helpful in determining the ultimate diagnosis.

If the IVP is suspicious or if there are clinical grounds for suspecting renovascular hypertension such as an epigastric bruit (31), renal arteriogram must establish the diagnosis (32). This must be followed by renal vein plasma renin activity assay in order to determine whether the lesion is a "significant" factor in the blood pressure elevation (33). It must be remembered that on the basis of chance alone, the incidence of mixed cases of essential plus renovascular hypertension will be at least 10 percent. The actual incidence, however, is much higher than this because essential hypertension predisposes to and accelerates atherosclerosis and an atherosclerotic plaque is the most common cause of renovascular hypertension. The existence of both diseases can be assumed if the tests for hereditary essential hypertension are positive as well as those for renovascular hypertension.

If there are clinical signs of Cushing's syndrome, this too must be confirmed by testing procedures such as the determination of urinary 17-hydroxysteroids (34) and ketosteroids (35) among other tests (36).

If the serum potassium is low, or the urinary output of potassium is abnormal on a fixed diet, then a low plasma renin activity will be needed to confirm the diagnosis of primary aldosteronism (37). This will require additional tests such as plasma aldosterone assay (38), urinary aldosterone excretion and/or secretion tests (39) and adrenal phlebogram (40). Again, the high incidence of associated hereditary essential hypertension must be remembered and assumed to be present if tests for this disease are positive. It is possible that essential hypertension may predispose to primary aldosteronism, since 50 percent of the patients successfully cured surgically, develop increased blood pressure again after several years without any recurrence of aldosteronism (41). There are rare forms of mineralocorticoid hypertension that are still under study and will require further testing. Before surgical intervention is recommended, for example, a trial of dexamethasone therapy is indicated to rule out one of the rare forms that responds to such therapy (42).

One of the most difficult problems in diagnosis is anxiety. This can produce sporadic or prolonged increase in blood pressure with or without associated tachycardia. In pure form, this condition is independent of hereditary essential hypertension (43). At least, the tests for the latter are all negative. Self-determined home blood pressures measured daily over long periods of time are normal in such cases. Of course, anxiety hypertension can be superimposed on essential hypertension and a positive test for the former, such as the response to isoproterenol (44) may become useful, although it is not in general use. Anxiety hypertension, however, yields to such therapy as reserpine, tranquilizers, and particularly propranalol.

The treatment for essential hypertension is usually confined to drug therapy today (45). The drugs used are compounds which deplete the body of either sodium or catecholamines as well as compounds which act directly on smooth muscle. It is unnecessary here to discuss such therapy in detail. It should, however, be emphasized that treatment should begin as early as possible, provided the diagnosis is established, and that prolonged and continued control by the physician is mandatory.

Summary

1. Hypertension is a widespread (epidemic) treatable disease.

2. Effective control requires case finding in the community backed up by relatively simple or extremely complex diagnostic procedures together with indicated individualized treatment.

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A Study of Mount Sinai Hospital Emergency Room Patients Seen by Psychiatric Residents

MORRIS H. BERNSTEIN, M.D. AND NORMAN STRAKER, M.D.

In recent years the emergency room (ER) of a general hospital has been increasingly used for the delivery of health services. This is especially true in deprived neighborhoods where there are few physicians in private practice. The trend is particularly apparent in the delivery of psychiatric services to the community. An increasing number of general hospitals are now equipped with emergency room "walk-in" facilities for psychiatric evaluation and treatment (1, 2, 3). Recently, these facilities have become more integrated with hospital and community needs. There is mounting concern and demand for early crisis intervention to prevent a break in homeostasis from progressing to the chronic stages (3). Since traditional methods of psychotherapy are not always applicable or effective for the population of the inner city and the psychosocial problems presented, new clinical and delivery techniques are necessary.

At The Mount Sinai Hospital the emergency room facility for psychiatry is presently located in a small office adjacent to the adult emergency room. Patients requesting to see a psychiatrist, or those referred by the emergency room staff, are required to wait in the crowded general emergency room waiting area. There are no nurses in the area specifically trained in psychiatry, no special facilities for handling a disturbed patient, and no beds allocated for psychiatry. Often, two to three hours may go by before patients are seen by a psychiatric resident who must leave his primary duties elsewhere; and some patients leave before being seen. The clerk at the registration desk is usually the person determining whether a psychiatrist is called. The decision is based upon request of the patient, a complaint of nervousness, or the clerk's observation of disturbed behavior. The resident on call is available for twenty-four hours and has access to the chief resident on call for consultation, but rarely consults him except for difficult dispositional problems, especially those cases requiring hospital admission.

Method of Study

This study is based on analysis of the emergency room consultation forms which are filled out for each emergency room consultation by the resident after seeing the patient. The completed forms are reviewed daily by the director of the Department of Psychiatry. The difficulties of analyzing the data from these sheets became obvious early in the study, and a new form is being drawn up based on these experiences. The new form will emphasize the multiple choice type of question which has many advantages, especially uniformity of response for coding purposes.

The sample used in this study is based on patient visits rather than individual patients. A patient visit is defined as one in which a patient is seen by the psychiatric resident in the emergency room. The study includes 962 visits in 1966, 1196 visits in 1967. This is compared at various times with a study of the total Emergency Room and Pediatric Acute Care facility with a total of 83,226 visits in 1967 (4). Our sample has been analyzed in terms of the following factors: area of residence, age, and method of referral of the visits.

A more detailed analysis of the visit sheets was made of 405 visits in 1967. This smaller sample is of consecutive patient visits from September 1967 to December 1967, in which diagnoses, problems presented, and dispositions were studied and cross-tabulated. These were the most recent visits at the time of our study.

A punch card was made for all patient visits. Although some sheets were lacking in information, were illegible or carelessly filled out, they were included and noted as such.

Results

Numbers and comparisons in total emergency room visits. The total number of psychiatric emergency room visits has increased from 962 in 1966 to 1,196 in 1967. In comparison with total ER visits, the number of psychiatric emergency visits is 1,196 of 83,226 = 1.4 percent. Although not documented as yet, visits in 1968 seem much higher (Table I).

Area of residence of patients. More than 50 percent of visits to the emergency room came from Manhattan in both 1966 and 1967. The largest single group of visits is from that part of Manhattan *not* designated as the hospital's catchment area, here defined as Manhattan north of 96th Street to 135th Street and east of Fifth Avenue. Only 19 percent of total visits came from the catchment area in 1967. In the study of the total ER visits, more than 53 percent are from

TABLE I

Psychiatric Emergency Room Consultation
Total Visits by Address Area

Area	Percent		
	1966	1967	1967S*
Catchment	17	19	19
Other Manhattan	40	38	35
Bronx	15	17	24
Brooklyn	11	11	9
Queens	6	7	7
Other	2	3	3
Not determined	8	6	3
	99% (962 visits)	101% (1196 visits)	100% (405 visits)

* 1967S are figures of the sample of 405 chosen for detailed analysis. They are presented here for comparison with total 1967.

TABLE II

Psychiatric Emergency Room Consultation
Total Visits by Age in Decades

Age in Decades	Percent		
	1966	1967	1967S
0–9	0	0	1
10–19	12	14	16
20–29	37	40	37
30–39	22	23	24
40–49	12	11	10
50–59	7	6	6
60–69	4	3	3
70–79	3	2	2
80–89	1	0	0
90–99	0	0	0
Not determined	2	1	1
	99% (962 visits)	100% (1196 visits)	99% (405 visits)

TABLE III

Psychiatric Emergency Room Consultation
Total Visits by Source of Referral

Source of Referral	Percent	
	1967	1967S
ER staff	7	11
Self	46	45
Friend or relative, not immediate family	3	3
Immediate family	9	10
Nonmedical professional	7	7
Medical (nonpsychiatrist)	12	13
Psychiatrist	4	4
Not determined	13	7
	101% (1196 visits)	100% (405 visits)

the catchment area, indicating that a different population is being served by the Psychiatric Service (4).

Age distribution. The age distribution is much as expected for the use of psychiatric services with more than one half of the patients falling in the 20–39 age range (Table II).

Referral source. The largest number of patients are self-referred: 46 percent for 1967 and 45 percent for the smaller sample. A surprisingly low 7 percent for 1967, and 11 percent in our small sample are referred by the ER medical staff, a

TABLE IV

Psychiatric Emergency Room Consultation
Total Visits by Major Diagnostic Categories

Major Diagnostic Categories	Percent 1967S
Organic Mental Syndrome	1
Schizophrenia	46
Affective Disorder	25
Neurosis	9
Situational Reaction	1
Character Disorder	4
Other	0
Medical	3
No Diagnosis	3
Not determined	7
	99% (405 visits)

total of 85 visits per year (Table III). This is all the more astonishing after referring to a study (4) of the total ER, in which 3.5 percent, or 1,635 visits were diagnosed as primarily "neurotic." The criteria for this diagnosis are not specified. It is apparent that very few of these were referred to the psychiatric resident (Table III).

Gross categories of diagnosis. Categories of diagnosis are presented in Table IV. In addition to information presented in Table IV, it should be noted that 15 types of depression were diagnosed, suggesting difficulties in following present nomenclature—a problem not restricted to our own residents.

Table V lists the *problems presented.* The predominant problems as stated on the sheet by the resident and (not necessarily indicative of the patient's chief complaint) are presented in Table V in order of frequency.

Disposition. Table VI illustrates the possible dispositions as they occurred in the ER. Thirty percent of patients seen in the emergency room are immediately hospitalized; 9 percent are admitted to our own hospital and 21 percent are referred to other hospitals. If we add to this the number of patient visits given in patient and Day and Night Center screenings—13 percent and 3 percent—a total of 49 percent are considered to be in need of hospitalization. From our statistics we can neither say with accuracy how many patients transferred or referred to another hospital either get there or were accepted there; nor do we know how many of the patients offered screenings actually were screened or accepted.

Cross-Tabulations. We also accumulated data to show the relation between presenting problem and disposition, as well as the relation between diagnosis and disposition. There were differences between patients hospitalized on an emergency basis at MSH and those referred to other hospitals. Patients referred elsewhere tended to show characteristics of anger, disturbed behavior, drug abuse, and to be suffering from chronic disease.

TABLE V

Psychiatric Emergency Room Consultation

1967S—Multiple*

Problem				No.	Percent
Previous psychiatric history				223	55
Fear				152	38
Depression				151	37
Somatic complaint				140	35
Not Suicidal					
Denies ideation		26	19		
No ideation		41	29	140	35
Not suicidal		74	53		
Problem with private life				130	32
Hallucination-Delusion				120	30
Disturbed behavior				104	26
Suicidal					
Ideation		63	66		
Attempt (Ingestive 9)		25	26	95	23
Risk		18	19		
Drug Abuse					
Major tranquilizer		5	6		
Minor tranquilizer		5	6		
Barbiturate		7	9		
Stimulant		1	1	82	20
Sedative		6	7		
Narcotic		4	5		
Alcohol		32	39		
LSD		6	7		
Marijuana		4	5		
Other or unspecified drug		31	38		
Relevant medical-surgical history				71	18
Not homicidal or denies	(H.	2	9)	59	15
No hallucination-delusion				62	15
Other problem (Including history of problem with private life, job, treatment or resistance)				55	14
Resistance to treatment				37	9
Neurotic symptom				32	8
Other minor psychiatric symptom				34	8
Wants inpatient care				28	7
Social Service or welfare history or problem				27	7
Problem with job				29	7
Problem with treatment				27	7
Addiction, including alcohol	(D.A.	26	32)	26	6
History of drug abuse	(D.A.	19	23)	25	6
Homicidal					
Ideation		18	78		
Attempt		2	9	23	6
Risk		6	26		
Suicidal history	(S.	16	17)	22	5
Sexual problem or history of				21	5
Wants care, OPD or unspec.				20	5
Anger				19	5
Wants medication				14	3
Suspicion				8	2
Homicidal history	(H.	1	4)	2	0
				(405 visits)	

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* Since some patients had multiple presenting problems, the total percent is greater than 100.

TABLE VI

Psychiatric Emergency Room Consultation

Sample 40—1967S Exclusive

Disposition	Percent
Outpatient screening	16
Inpatient screening	13
Day and Night Center screening	3
Unspecified screening	5
Emergency admission	9
Refer to other hospital	17
Refer to other hospital plus MSH screening	4
Refer to private doctor	1
Return to previous care	14
Medical consultation	7
Medication	5
Other disposition	1
No disposition	0
Not determined	2
	97% (405 visits)

Medications. The final table (Table VII) shows the kinds of medications prescribed by the psychiatric residents for the 405 patients in the sample.

Conclusions

Our study of adult psychiatric patients in The Mount Sinai Hospital emergency room shows functional isolation of the psychiatric emergency service from the rest of the psychiatric service, and also from the rest of the ER facility. This is demonstrated by the small number of referrals from ER staff to emergency psychiatry (less than ten percent of psychiatric ER patients), by the large number of dispositions made outside Mount Sinai, and by the absence of teaching and supervision in ER by the psychiatric attending staff. The home address of psychiatric patients seen in the ER indicates that a city-wide clientele is being serviced, rather than patients from the MSH catchment area who represented less than 20% of the total.

The characteristics of the adult psychiatric patients seen are as follows: half are age 20–39; 45% are self-referred to the psychiatrist; 46% are diagnosed as schizophrenic. The most common presenting problems are fear (38%), depression (37%), somatic complaints (35%), hallucinations and delusions (30%). In disposition, a total of 49% are referred for hospitalization; 21% to other hospitals.

Discussion and Recommendations

Many psychiatric as well as medical patients now use the ER as their primary source of care (5). Emergency rooms are being used more, and for

TABLE VII

Psychiatric Emergency Room Consultation

1967S Exclusive

Medication	Visits	Percent
Antidepressant	14	10
Major tranquilizer	49	34
Minor tranquilizer	18	13
Barbiturate	8	6
Stimulant	0	0
Sedative	7	5
Narcotic	0	0
Miscellaneous or unspecified	9	6
Antidepressant plus major tranquilizer	22	15
Antidepressant plus major tranquilizer plus other	2	1
Antidepressant plus other	2	1
Major tranquilizer plus other	13	9
Rx if medical evaluation negative	0	0
		(100)
Subtotal	144	36
Discontinue Medication	1	0
No Reference to Medication in Disposition	260	64
Total	405	(100)

purposes they were never designed to meet. The ER must move in one of two directions: limit itself to handling true emergencies, or adapt itself to the requirements of providing acute care on a drop-in basis (6).

Recent experience of a psychiatrist in a comprehensive ambulatory health care program at MSH indicated the feasibility of providing psychiatric care for the East Harlem ghetto population on a drop-in basis. Although patients were originally offered definite appointments, most of them felt free to skip a scheduled appointment for no particular reason, and equally free to drop in without an appointment after they knew the psychiatrist. All staff members, both professional and nonprofessional (indigenous health aides) worked in close collaboration, and much of the actual treatment of the psychiatrist's patients was delegated to nonpsychiatric staff members. In this way a team approach was developed which permitted some turnover of staff as long as a solid cadre of staff members remained at all times. A regular patient of the unit could always find staff members who were familiar to him, and strong personal ties developed (7).

On the basis of this experience, and of the present study, we believe the emergency room should provide emergency care and acute care on a drop-in or appointment basis, provided by a psychiatric staff at the attending and resident level, case workers, nurses, and health aides, all of whom have the ER as a major responsibility, and are prepared to devote a bloc of time on a regularly scheduled basis to the work there. The psychiatric staff should be well integrated with the medical staff. In addition the psychiatric staff should perform the function of triage for patients who seek primary care in the ER. This requires a thorough knowledge of community resources in addition to the hospital's own resources. Triage by a highly trained professional staff is performed on the basis of careful evaluation, and is completely different from the sorting function which can be performed by a clerk (8).

The ER facility should include a few beds in a separate area so that acutely disturbed patients can be observed and treated by the staff for periods up to 72 hours, without the requirement of formal hospital admission. Many admissions can be prevented with this type of service (9).

Administrative and case conferences should be scheduled regularly; the work should be subjected to regular and systematic review by senior members of the various departments. Since our study shows that not all patients with emotional problems are being seen by a psychiatrist in our ER, a psychiatrist should participate in the review of nonpsychiatric visits. And certainly those patients who make frequent or regular use of the ER should have psychiatric evaluation.

Another issue is that as psychiatrists we have had difficulty providing help for the inarticulate, unreflective citizens of inner city slums. We must have an awareness and respect for the patients' cultural traits and values. These patients are not prepared by anything in their backgrounds, and they see no relevance in a series of scheduled visits to a health professional. It requires too much organization of personal life, advance planning and negotiating, and submission to authority (10). These patients want help when something hurts, either physically or emotionally.

Summary

In this presentation we have described the functioning of The Mount Sinai Hospital Emergency Room with respect to psychiatric patient visits.

Suggestions were made to improve staffing pattern and procedures, physical characteristics, and record-keeping.

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Noise and Health

SAMUEL ROSEN, M.D.

Many studies have shown that continued exposure to loud noise not only can damage the ear but can have other harmful effects. In heavy industry, neurosensory hearing loss induced by noise occurs frequently and is irreversible, although protective devices may help to postpone and to slow the development of such loss. In some areas of industry a recognition of this problem exists, but little has been achieved in the way of its solution.

But what about the constant noise of everyday life in our highly mechanized society? What happens to the average urban and suburban resident who is exposed to the roar of traffic, aircraft, sirens, motocycles, heavy trucks, jackhammers, pneumatic riveters, outboard motors, heavy farm equipment, subways, power lawn mowers, home appliances of all kinds, and rock music? Consider these noises compounded with the clamor of people talking loudly and, perhaps, shouting at the same time. Such noise invades our daily life whether we are awake or asleep, and we are helpless against it.

There is an interesting case in point reported by Philipszoon (1) of Amsterdam, Holland, concerning an 82-year-old man who came to the outpatient department for a hearing aid. The right ear drum was found to be normal, but deep in the left meatus the doctor found a large brownish mass which resisted removal by syringe. It was finally removed with a sharptoothed forceps, and proved to be a dirty piece of cotton which had completely obstructed the auditory canal. It was revealed that the patient had been treated 32 years earlier for otitis. The family doctor had neglected to remove the cotton and had overlooked its presence in the ear. Thus Philipszoon had a controlled experiment in the same individual, with one ear noise-exposed and the other protected for 32 years by the mass of cotton. The audiogram showed the expected presbycusis in the right ear, a pure perceptive deafness. The loss was much less in the left ear, showing a mixed, or perceptive and conductive deafness (Fig. 1). The bone conduction was much better in the left ear than in the right.

One may surmise from this case that the noise of everyday life is a very important factor in hearing loss due to aging. Presbycusis is generally more pronounced in men, since they are more exposed to noise than women. However, in our studies in the African jungle, where all the people live in virtual silence, we found that the Mabaan men hear as well as the Mabaan women (2).

The effect of noise can also change the physiologic state. Since we believe that extreme physiologic changes are a health hazard, we must also consider noise a health hazard. A sudden noise causes a number of reactions in the body. In addition to the primary psychic shock, one winces, turns the head, holds the

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Emeritus Clinical Professor of Otolaryngology, Mount Sinai School of Medicine of The City University of New York, N.Y. 10029; Consulting Otologist, The New York Eye & Ear Infirmary, New York, N.Y.

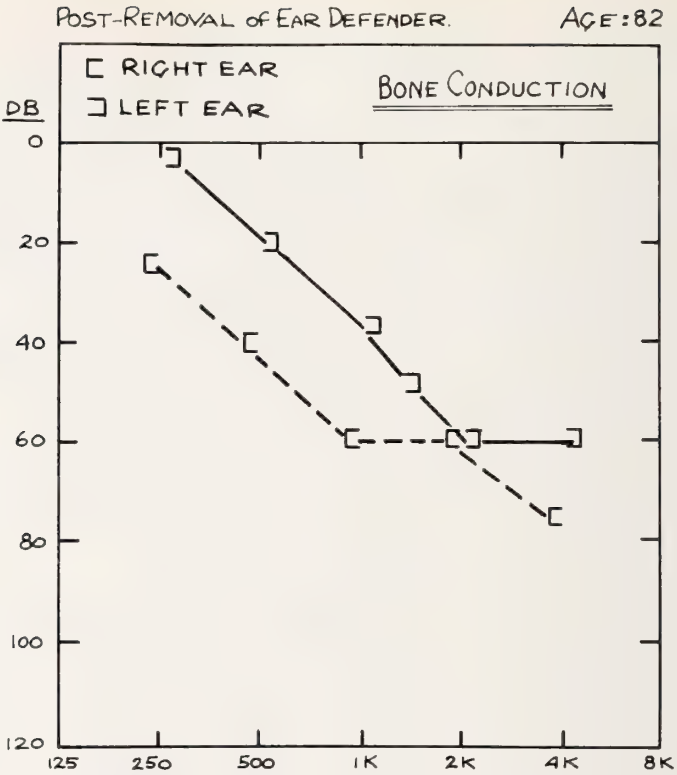

Fig. 1. Post-Removal of Ear Defender. Age: 82.

breath, closes the eyes briefly—then breathing is accelerated, the pupils dilate, the skin pales, and adrenalin is poured into the bloodstream.

Studies have shown that a sudden noise affects the vegetative nervous system, an important function of which is the regulation of the caliber of the blood vessels. Lehman and Tamm (3) found that peripheral resistance, or vasoconstriction of the precapillary vessels, increased at the onset of noise and persisted even longer than the noise. This peripheral vasoconstriction was recorded plethysmographically by a cuff at the end of the finger. Jansen (4) has shown that during a noise period of five minutes a sharp 24 percent fall in the curve is seen, significant of vasoconstriction. Following this five-minute period of noise, vasoconstriction begins to dissipate, but may linger as long as 25 minutes. During vasoconstriction there is a diminution in cardiac output and an increase in diastolic pressure.

The greater the noise intensity and band-width the greater the vasoconstriction, during sleep as well as wakefulness. The increase of noise intensity and the increase of vasoconstriction are proportionately linear. In our African study the intitial vasoconstriction was greater in the Mabaans than in subjects in Germany (Fig. 2). Coronary heart disease and hypertension are unknown among the Mabaans. Their hearing with aging is superior to ours.

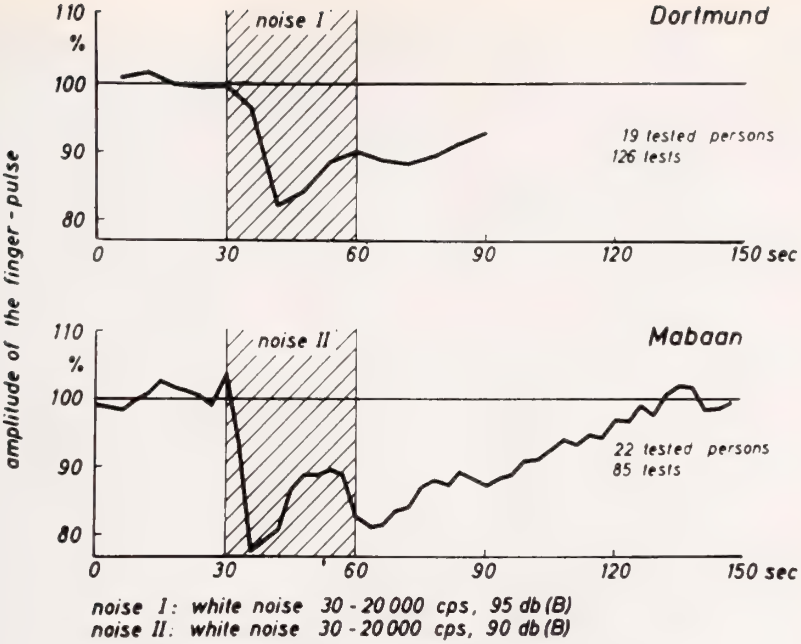

FIG. 2. Comparison of Vasoconstriction. Dortmund & Mabaan.

Personality differences, of course, result in different degrees of annoyance and irritability—but the peripheral vasoconstriction was observed in all cases at whatever intervals the noise was delivered. It was also seen in those subjects previously accustomed to similar noise. Subjects who had been told when the noise would begin were unable to prevent or control the vascular reaction. We may become used to the noise, but our blood vessels never do.

Raab (5, 6, 7) has shown that even mild sensory and mental annoyances which occur in everyday life, like noise, for example, may provoke significant elevations of plasma cortisol level accompanied by increased heart rate and blood pressure, especially in emotionally excitable individuals. In view of the well-known potential metabolic cardiotoxicity of combined catecholamine and glucocorticoid overreaction, these neurogenic and hormonal stress responses have implications related to human myocardial pathology.

Noise is a centrally mediated stress. The end effect of various stresses in promoting the production of scattered myocardial lesions can be ascribed to hypoxic or anoxic changes in the ventricular tissue under the influence of primarily metabolic and or primarily microcirculatory alterations which are elicited by the sympathetic nervous system. Adrenergic catecholamine discharges into the blood (epinephrine from the adrenals) and or directly into myocardial cells (norepinephrine from the sympathetic nerve terminals) occur under emotional as well as under sensory stresses. Since augmented catecholamine action is associated with an increased oxygen consumption by the heart muscle, local hypoxia may develop in myocardial areas whose oxygen supply is

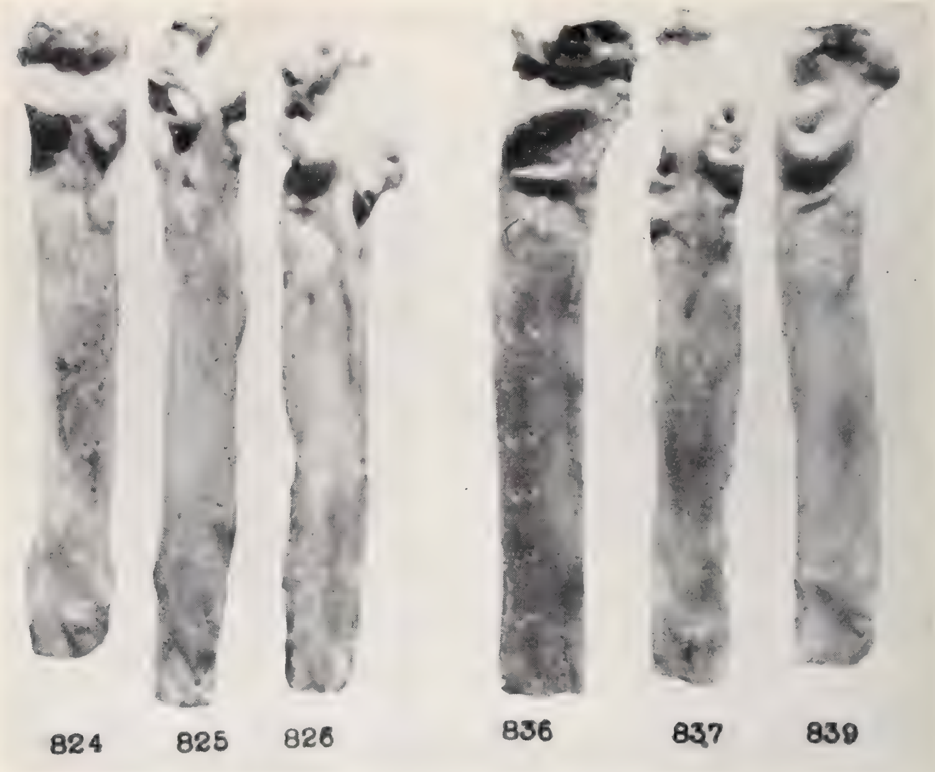
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FIG. 3. Aortic atherosclerosis in noise-exposed animals.

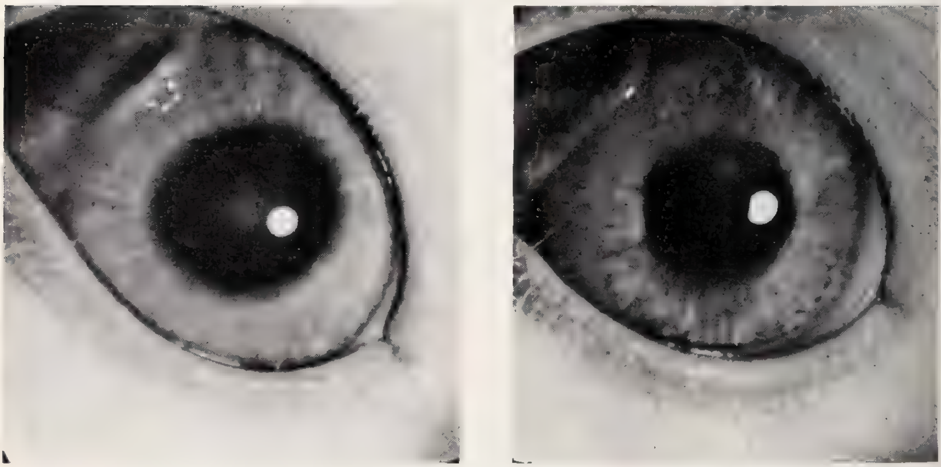

FIG. 4. Cholesterol deposits in the iris in noise-exposed animals.

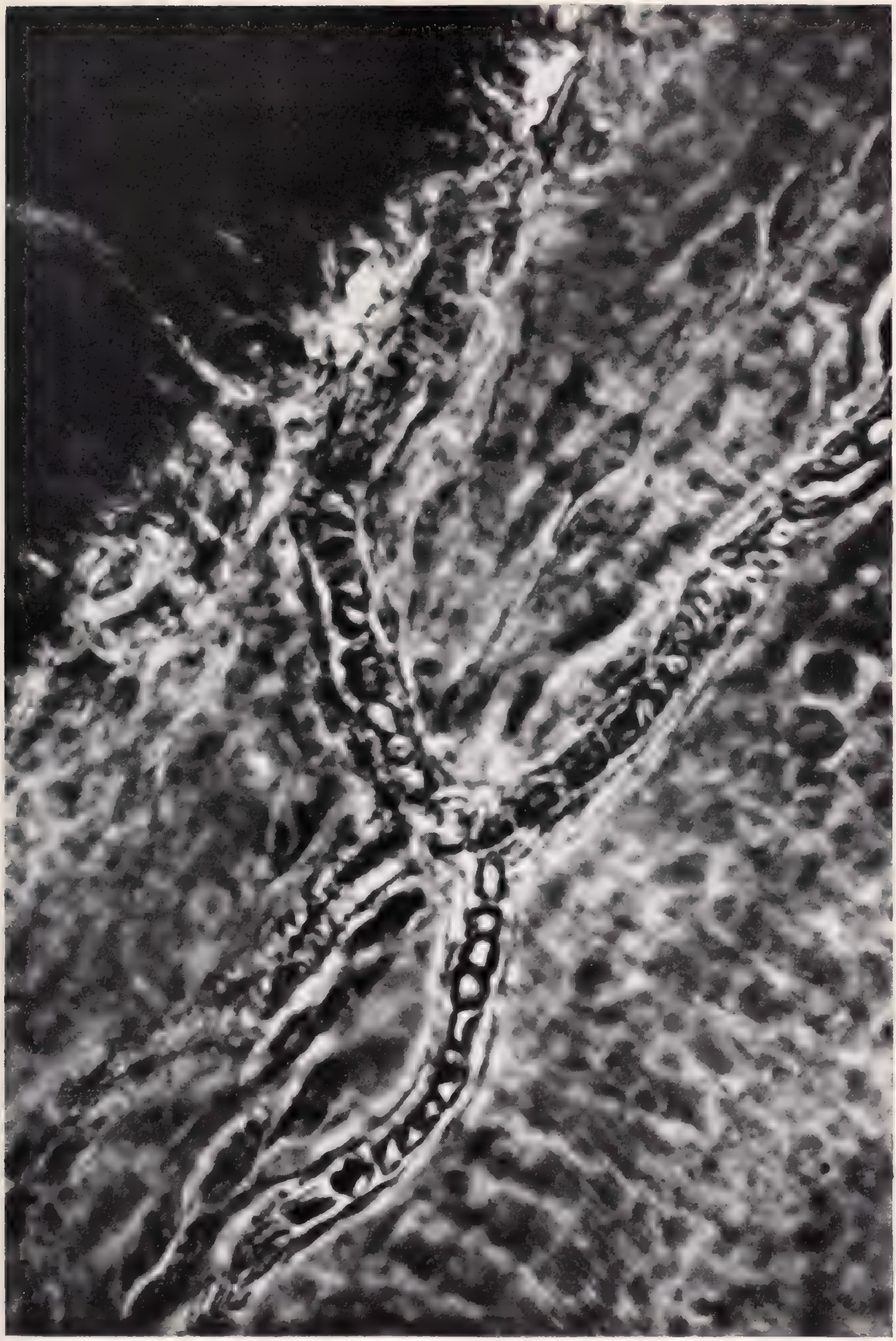

FIG. 5. Before Vasoconstriction of cochlear vessels.

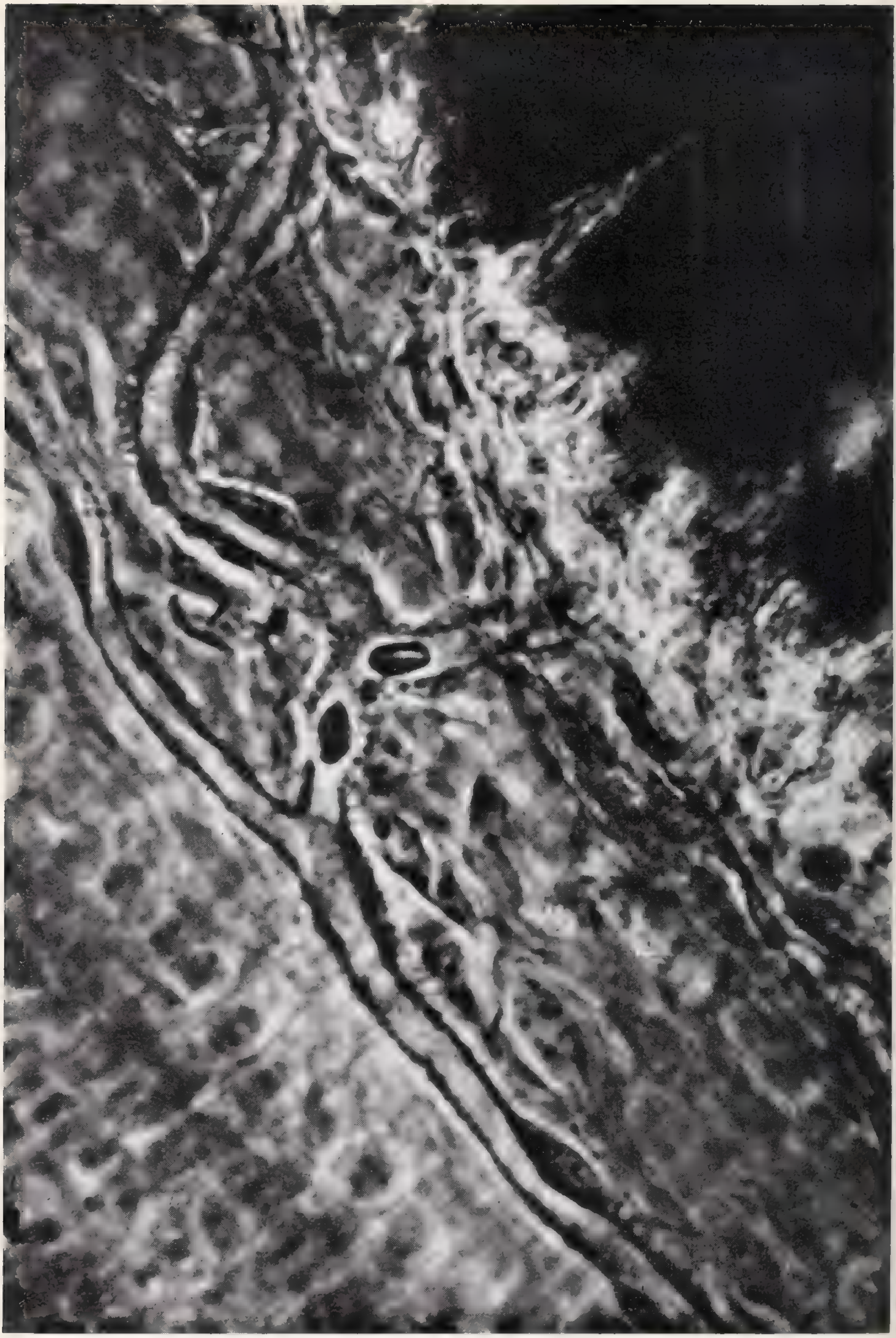

Fig. 6. Vasoconstriction of cochlear vessels.

handicapped by inadequate compensatory dilatability of the supplying coronary vascular branches. This is the case in the presence of coronary arterial or arteriolar sclerosis and also when the intraventicular hemodynamic pressure rises under catecholamine action, thus exposing the particularly vulnerable subendocardial layers of the left ventricle to hypoxia-producing local vasocompression. Myocardial hypoxia, in turn, always causes a local loss of vitally necessary potassium and magnesium, paralleled by a potentially cardiotoxic increase in cellular sodium.

Endocrine responses to loud sound in man were measured by Arguelles (8) of Argentina, who exposed normal, hypertensive, postmyocardial infarction and schizophrenic subjects to a pure tone of 2,000 cps at 90 db intensity. His studies confirmed some earlier results obtained elsewhere that noise stimulation elicits a marked epinephrine and norepinephrine rise in peripheral blood, particularly in the postinfarction and hypertensive subjects.

Now let us look at animal experiments. It has recently been shown by Friedman et al (9) that rabbits exposed to 102 db of white noise for 10 weeks showed a much higher level of blood cholesterol than similarly fed animals not exposed to noise (Fig. 3). The noise-exposed animals developed a greater degree of aortic atherosclerosis with higher cholesterol content. Also, cholesterol deposits in the iris were more severe and extensive in the noise-exposed animals (Fig. 4).

Lawrence, Gonzalez and Hawkins (10) demonstrated histologically in animal experiments that noise causes vasoconstriction of the cochlear vessels, particularly in the spiral vessels underlying the basilar membrane and the stria vascularis, accompanied by a significant reduction in the flow and number of red blood cells reaching the Organ of Corti (Fig. 5 and 6). This vasoconstriction of the cochlear vessels probably causes ischemia, or anemia, and the sensory cells show structural changes leading to loss of function.

Such investigations as I have described appear to point to noise as an environmental pollutant as well as a health hazard. The psychic effect of noise is also very important. It can cause enough emotional response and frustration to make people feel nervous, irritable, and anxious. Life in this world is so full of stress and strain that every possible effort must be made to eliminate those which are amenable to elimination. The reduction of noise levels in everyday life is not an impossible dream. Many sources of high-level noise can be made quieter through proper engineering techniques and the application of acoustical science and technology, and through effective governmental regulation and control.

As physicians aware of the danger to health, we should all be involved in the campaign against noise pollution, just as we are all enlisted in the struggle against disease.

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Studies in Myasthenia Gravis: Review of a Twenty-Year Experience in over 1200 Patients

KERMIT E. OSSERMAN, M.D. AND GABRIEL GENKINS, M.D.

The Myasthenia Gravis Clinic at The Mount Sinai Hospital in New York City opened in 1951 with a modest six patients on our roster. The Clinic now registers over 1200 patients, approximately 3000 annual visits, and 75 to 100 hospital admissions per year. We are endeavoring to better understand the diagnostic, therapeutic, and clinical aspects of a disease which, as yet, eludes total understanding. Gratifying advances in recognition and therapy have occurred, but much remains to be done.

Incidence of Myasthenia Gravis

Although not a rare disease, myasthenia gravis is still uncommon. The best estimates approximate an occurrence rate of 1/20,000 population (1), but the true incidence is probably higher. There is no known endemic area, no socioeconomic predeliction, no occupational or known exposure correlation -indeed nothing of a specific epidemiologic nature. No ethnic predominance has been noted (2).

Age and Sex

No age from cradle to grave has been spared, but there are distinct peaks of sex and age incidence.

The predominant onset rate in young females in their third decade led to some early therapeutic approaches and misconceptions. As noted in the figure, the mode rate for males causes equalization of disease onset in the two sexes in the fifth and sixth decade. The total patient population appears to be weighed 6:4 in favor of the females.

Genetics

Genetic and familial studies are incomplete, but we and others have noted significant incidence of multiple disease in one family grouping. In our series about 5 percent of our total patient group were related to each other.

These data are not sufficient to indicate any genetic or inheritable pattern, and the neonatal group described subsequently in no way denotes this.

Of those cases cited in the literature, six families were reported either by Osserman (3) or by others (4, 5) based on The Mount Sinai Hospital population. Since these reports, we have accumulated twenty-five additional families

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From the Department of Medicine and The Myasthenia Gravis Clinic and Research Laboratory of Mount Sinai School of Medicine of The City University of New York, N.Y. 10029.

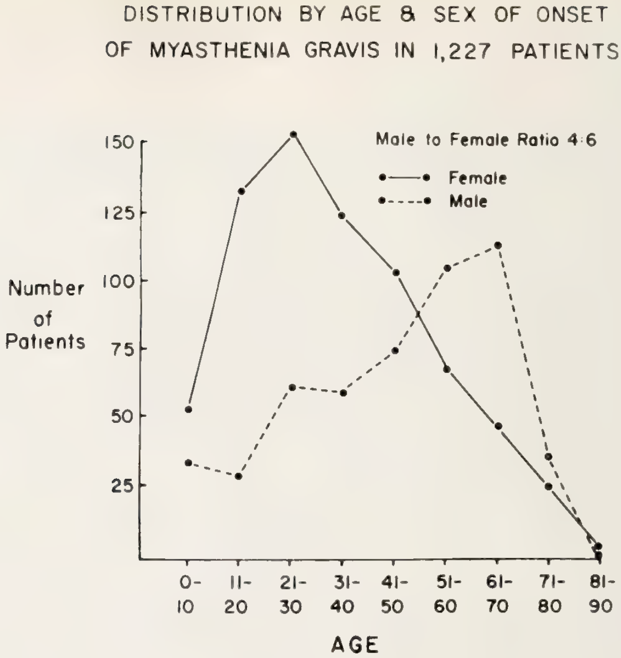

Fig. 1.

with more than one member affected by myasthenia gravis. In sixteen families, the myasthenic patients were seen at the Myasthenia Gravis Clinic and the diagnoses were confirmed. In fifteen other families, only one member was so confirmed; the others were inferred by history, with confirmation made by competent examiners not at The Mount Sinai Hospital. In this group seven patients were of two generations. We have now studied three families in depth (at least three generations) in which more than one myasthenic exists and one family in which there is no myasthenia or other autoimmune disease. We have sought by indirect immunofluorescence, tanned-red-cell muscle hemagglutination, and Ouchterlony precipitin tests to find the presence of muscle antibody in these families, as compared to our entire myasthenic population, as well as to our control sera of normal individuals and of patients with neurologic diseases and other autoimmune disease. Preliminary results point to a much higher incidence of positivity by at least one of the three tests used in the sera of families with known myasthenia. Further collection of larger numbers of normal control family sera as well as other genetic studies are being performed. Myasthenia gravis is more common in families than probability alone would suggest but not frequent enough to support clearly genetic determinants.

Associated Diseases

Scrutiny of clinical features in this disease has shown an increased incidence of other morbid states, some possibly "autoimmune" in type. Thus far there is no possible significance to be ascribed to such association other than the notation of their occurrence, apparently far beyond random chance in a total population. We find that in our myasthenic group there are 13 percent of patients with thyroid anomalies of which one-half were hyperthyroid (6); 6 percent were diabetic; 3 percent had rheumatoid arthritis; 0.5 percent had systemic lupus erythematosus; 0.5 percent had leukemia (7); 0.5 percent had pemphigus (8); 0.3 percent had scleroderma (8); and almost 1 percent had polymyositis (9) and seizure disorders and an apparent major absolute increase of various malignancies (7.5 percent), especially breast carcinoma (10). Again, it is interesting to note the autoimmune classification of a number of these diseases.

It has been noted in our laboratory that each of these morbid states has an incidence of antinuclear factor with seropositivity between 20 and 30 percent demonstrated. When myasthenia gravis is concomitant with an autoimmune disease, seropositivity ranges between 90 and 100 percent, similar to its almost ubiquitous presence in systemic lupus erythematosus.

Certain other conditions such as functional bowel disease and peptic ulcer may be related both to stress of a chronic life threatening state and to the long-term use of cholinergic drugs.

Symptomatology

Myasthenia gravis is a syndrome characterized by increased muscle weakness upon repetitive use of involved groups and by partial return of function with rest and administration of appropriate drugs. Voluntary striated muscle is involved. The cardinal symptom of myasthenia gravis is weakness involving one or more striated muscle groups. The weakness becomes more evident on prolonged or repeated use of the muscle (11). One of the most common signs of myasthenia gravis is unilateral or bilateral ptosis. Frequently the ptosis shifts from one eye to the other (12). Although ptosis may be the only evident sign of myasthenia gravis, systemic examination may reveal unsuspected weakness or fatigability in muscles other than those apparently involved. In most patients, ptosis is accompanied by diplopia and blurring of vision. The ocular signs and symptoms are frequently made worse by bright light. Occasionally, patients report that sunshine causes an increase in the severity not only of ocular manifestations but also of other signs and symptoms of myasthenia gravis (11). Another frequent sign is the myasthenic facies caused by weakness of facial muscles. This is also responsible for the "vertical snarl" which develops when myasthenic patients are asked to show their teeth. Weakness of jaw muscles may cause difficulty in chewing, becoming more difficult as the meal progresses. In many patients this makes consumption of any solid food impossible. Chewing difficulties are often accompanied by dysphagia. Not infrequently, the first manifestation of dysphagia is nasal regurgitation of fluids. Difficulties of speech are commonly encountered in myasthenic subjects. Myasthenic dysarthria is characterized by a nasal twang. When starting to speak the voice may be relatively clear and easy to understand. Later the volume of the voice decreases and its clarity diminishes (13).

Inspiratory distress may be the first recognized sign of myasthenia gravis. Whether the dyspnea is primarily inspiratory or expiratory depends on the muscle groups involved. With diaphragmatic involvement, the dyspnea is inspiratory. When the intercostal and abdominal muscles are affected, the dyspnea is primarily expiratory. In milder cases dyspnea only occurs during exercise. There is a relatively good correlation between the patient's vital capacity and his exercise tolerance. Maximal breathing capacity diminishes out of proportion to the decrease in vital capacity. A relatively uncommon sign of the disease is a triple longitudinal furrowing of the tongue, called the "myasthenic tongue" (14).

The most frequently involved skeletal muscles are those of the neck, shoulder girdle, and hip. The proximal leg muscles are affected more often than the distal ones. The extensors of the upper extremities are usually more involved than the flexors. There can be marked difference in the strength of the two upper extremities. Involvement of the lower extremities is usually more symmetrical.

Early atrophic changes of involved muscle groups occur more frequently than formerly believed. Atrophy, especially that of the quadriceps femoris, may occur as early as six months after the onset of myasthenia gravis (15–17).

Sensory changes both in involved or uninvolved muscle groups are frequently present in myasthenia gravis. Patients usually have little discomfort in the morning but the pain becomes more severe as the day progresses. Frequently, rest or anticholinesterase medication will give relief. The pain, in part, may be due to the extra effort required to maintain posture with the weak muscles. Other sensory changes encountered are headache, ocular pain, and paresthesias

TABLE I

Incidence of Symptoms

	At Onset	Current Status
Ocular		
Diploplia	43%	73%
Ptosis-Bilateral	27%	59%
Ptosis-Unilateral	40%	25%
Bulbar		
Dysarthria	27%	61%
Dysphagia	23%	63%
Chewing Weakness	16%	52%
Dyspnea	6.5%	33%
Skeletal		
Generalized Weakness	15%	45%
Facial Weakness	8.5%	38%
Neck Weakness	9%	40%
Trunk Weakness	3.5%	14.5%
All Extremities	10%	44%
One or Two Extremities	25%	45%
Atrophy	–	6.3%
Subjective Sensory Symptoms		9%

of the face, lips, tongue or extremities (18). In an earlier report from this institution, sensory changes have been observed at one time or another in about 14 percent of our cases (19).

Clinical Classification

Classification of the patients into definable clinical groups makes it difficult to maintain a unitarian disease concept. These groups behave in significant and predictably different patterns. We have thus come to prefer the term "syndrome" rather than disease. It must be emphasized that this classification is dynamic and not static, but that time elapsed and muscle group involvement as described below do permit prognostic statement and do dictate therapeutic approach. Over 1200 patients form the basis for this classification which has been adopted by most major clinical centers, including the clinic of The Massachusetts General Hospital (20). Myasthenic patients have been divided into a pediatric and an adult group.

PEDIATRIC GROUP

Neonatal group. Neonatal myasthenia gravis occurs only in infants born of myasthenic mothers and is a self-limited condition lasting no more than six weeks. It is probably caused by the transmission of a serum factor across the placental barrier. Progression to juvenile myasthenia has been reported in only one instance (21).

Juvenile group. Unlike the neonatal form, clinical myasthenia is not present in the mothers of the affected children. Juvenile myasthenia tends to be permanent and may develop at any time from birth to puberty. In those infants in whom the disease begins at birth, there may be an apparent confusion with the neonatal form, but the mother's status and the permanence of the defect soon define the actual classification. Siblings and close relatives of juvenile myasthenics may also have the disease. Bilateral, partial, or complete ophthalmoplegia with severe ptosis, often resistant to drug therapy, is common in this group. Symmetrical limb involvement is also frequently present. The nature and degree of the myasthenic defect dictate classification of these patients into the more descriptive divisions of the adult groups below.

ADULT GROUP

Adult myasthenic patients have been divided into four groups. *Group I: Ocular Myasthenia.* This localized form of the disease is maybe limited to only one eye and characterized by ptosis and diplopia. This group has an excellent prognosis, and if there is no spread of the myasthenic involvement to other muscle groups within two years of onset, the disease usually remains nonprogressive.

Group IIA: Mild Generalized Myasthenia Gravis. This group is characterized by slow onset, frequently ocular, gradually spreading to the skeletal and bulbar musculature. Respiratory muscles are spared. Response to drug therapy is good and mortality is very low.

Group IIB: Moderate Generalized Myasthenia Gravis. In this group the onset is gradual, with frequent ocular presentation, progressive to a more severe generalized involvement of skeletal and bulbar musculature. Dysarthria, dysphagia, and poor mastication are more prevalent than in Group IIA but the respiratory muscles are again not involved. Response to drug therapy is less satisfactory and the patient's activities are restricted. Mortality is low.

Group III: Acute Fulminating Myasthenia Gravis. Rapid onset of severe bulbar and skeletal muscle weakness with early involvement of the respiratory musculature characterizes this group. Progression of the disease is usually complete within six months. The percentage of thymomas is highest in this group. Response to drugs is poor; and the incidence of myasthenic, cholinergic, and brittle crises is high. Mortality is also high.

Group IV: Late Severe Myasthenia Gravis. In this group, severe myasthenia gravis develops at least two years after onset of Group I or II symptoms. The progression of the disease may be gradual or sudden. This group has the second highest percentage of thymomas. Response to drug therapy and prognosis are poor.

Some patients in Groups II and IV may demonstrate localized muscle atrophy, not correlated with disuse, and not associated with any demonstrable lesions of the central and peripheral nervous system. Electromyography of the involved muscle groups reveals a characteristic myopathic pattern.

Diagnosis

The diagnosis of myasthenia gravis in a patient with classic symptoms is simple. In its milder forms, especially early after onset, the diagnosis may be difficult. A high degree of suspicion of myasthenia gravis is necessary. Careful attention to the patient's history is of paramount importance. One must seek information regarding the onset of weakness and its diurnal variation, effect of rest, influence of the menstrual cycle, infection, emotional stress, response to medications, and tolerance of ordinary and extraordinary physical activity.

TABLE II

Distribution of Myasthenic Patients by Clinical Classification

	No of Patients	Percentage
Pediatric		
Transient Neonatal	20	1%
Juvenile	111	9%
Adult		
Group I	246	20%
Group II A	357	30%
Group II B	249	20%
Group III	136	11%
Group IV	111	9%
Total	1230	100%

Frequently there is a history of early remissions with subsequent exacerbations. The shift of ptosis from one eye to the other is almost pathognomonic of the disease (22). Critical attention must be paid to the objective assessment of the alleged weakness. This will make possible the exclusion of neurotic asthenia which may closely mimic myasthenia gravis.

Thorough physical and neurologic examination must be performed with the patient in a basal state (nonmedicated). For borderline cases provocative physical activity may be necessary to demonstrate muscle weakness. Routine laboratory procedures are generally unrevealing. Specific studies such as chest radiography (with tomography if indicated), thyroid evaluation, lupus erythematosus preparations, and immunologic testing of serum may be helpful. The finding of thymic enlargement is common in myasthenia gravis.

Pharmacologic tests of a reparative and provocative nature with or without electromyography and ergography will resolve most diagnostic uncertainties. Edrophonium (23), neostigmine (24), d-tubocurarine (25), and decamethonium (26) are the drugs used in these procedures. Quinine (27), previously advocated as a provocative test, is hazardous and should be avoided (28).

When isolated weakness of a specific muscle group such as the pharyngeal constrictors is present, fluoroscopic examination during swallowing of contrast media before and after administration of anticholinesterase drugs is often helpful. In order to rule out false positive response, all drug tests must be evaluated against a placebo response, preferably in a double blind fashion.

EDROPHONIUM TEST (Tensilon®)

The edrophonium chloride diagnostic test for myasthenia gravis was developed by Osserman and Kaplan (29). In its present form the edrophonium test is performed as follows (30): The patient's muscle strength is assessed by both subjective and objective methods (e.g., dynamometer and ergograph), with special attention paid to muscles involved in the myasthenic process. Vital capacity is measured with a ventilation meter, and chewing and swallowing are observed. After a rest period of five minutes, 2 mg of edrophonium are injected intravenously, and muscle performance is again assessed within 30 to 90 seconds. If this dosage of edrophonium does not result in adequate response, 3 and 5 mg increments should be tried 3 minutes apart. If the 2 mg dosage gives a cholinergic response (see later) the test should be repeated 30 minutes later with a 0.5 to 1.0 mg dosage. The edrophonium test in a patient with oculobulbar myasthenia gravis is illustrated in Figure 2. If it is suspected that the weakness is not myasthenic but is functional or is caused by other muscular or central nervous system diseases, the administration of edrophonium should be paired in a double blind fashion with intravenous injection of a placebo. Either 20 mg nicotinic acid, 200 mg calcium chloride, or 0.3 to 0.4 mg atropine may be used for this purpose (31). The edrophonium test has several advantages. It can be repeated within 10 minutes; its effect develops rapidly and wears off quickly so that both examining physician and patient have the opportunity to observe repeatedly the effects of anticholinesterase medication. The incidence and se-

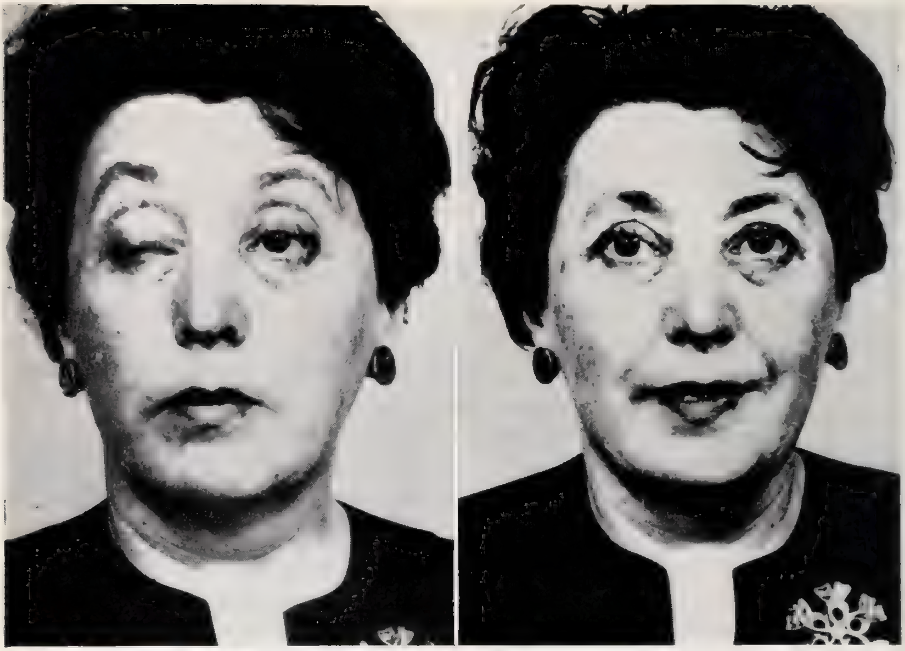

FIG. 2. Response to edrophonium test. *Left,* before edrophonium test; patient showing ptosis and lack of facial expression. *Right,* thirty seconds after edrophonium test; ptosis relieved and patient's expression normal. Reprinted from *Myasthenia Gravis* by K. E. Osserman, M.D. Permission granted by Grune & Stratton, New York and London.

verity of muscarinic side-reactions are much less than after an injection of neostigmine, and, if they do develop, wear off rapidly.

CURARE TEST

In an occasional patient, with mild generalized myasthenia gravis, the information obtained from the edrophonium or neostigmine test may be equivocal. In such patients further information may be obtained by use of d-tubocurarine (25, 32) or gallamine (33). Because of the well-known sensitivity of myasthenic subjects to even very small doses of d-tubocurarine, extreme caution is necessary when this test is employed. Its use should be limited to those cases where definite diagnosis cannot be obtained with the edrophonium or neostigmine tests. It is essential that drugs and equipment necessary for respiratory resuscitation, as well as physicians well versed in their use, be at hand when this test is performed.

Baseline electromyography (Jolly test) is carried out and equipment left in situ. If this reaction is negative, namely, no fall-off is noted on repetitive stimulation, one proceeds with administration of curare, intravenously, using the following dosage schedule and technique:

With the patient recumbent, an intravenous infusion is started. Objective and subjective signs of muscular weakness are assessed, just as before an edrophonium test. The curarizing dosage for normal individuals averages 3 mg per 40 pounds of body weight. A total of one-fifth of the amount thus arrived at is diluted in a 10 ml syringe with normal saline. Progressive aliquots of 1, 2, 3, and 4 ml are given every two minutes with clinical evaluation at one minute after each dose and electromyographic testing just before the next dose. A positive clinical or electromyographic finding signals the end of the test no matter at what dosage level it may occur. At this point the curare effect is to be antagonized and repaired by intravenous administration of edrophonium followed by neostigmine. While a few (4 percent of normal subjects) may demonstrate false positive reactions, the test otherwise is highly diagnostic and specific in this dosage range.

In order to avoid systemic curare response and possibly resulting respiratory collapse, this test may be performed by a regional method. Intravenous injection of 0.2 mg of curare diluted to 20 ml of saline is performed with proximal pressure occlusion of the extremity above systolic levels for six minutes (34). Dynamometer, ergograph, or electromyographic readings are taken and compared to baseline levels previously recorded. Purely ocular myasthenia (Group I) escapes definition by this technique.

DECAMETHONIUM TEST

The myasthenic muscles' unusual resistance to decamethonium has also been employed in a diagnostic fashion (26, 35). Because uninvolved musculature may be normally sensitive, resulting in unexpected respiratory and vascular collapse without available antagonists, we prefer not to use this modality.

Treatment

Because of its unknown etiology, the treatment of myasthenia gravis is empirical. The various therapeutic measures employed include drugs, surgical removal of the thymus, and radiation therapy.

DRUG THERAPY

Drugs employed in the management of the myasthenic patient may be divided into two groups, anticholinesterase drugs and adjuvant drugs. In addition drugs may also be required to counteract the unwanted side-effects of anticholinesterase medications.

Anticholinesterases. The anticholinesterase drugs usually employed in the treatment of myasthenia gravis are relatively short-acting mono- and biquarternary ammonium compounds. Biquarternary ammonium compounds with relatively long duration of action and the even longer acting alkylthiophosphates are only rarely employed in the treatment of the disease. Consequently, only the clinical use of the short-acting quarternary ammonium type anticholinesterases will be discussed in detail (36).

Anticholinesterase drugs such as neostigmine bromide (Prostigmin®) (37), pyridostigmine bromide (Mestinon®) (38–42), and ambenonium chloride

(Mytelase®) (43–45) greatly help to correct the defect at the neuromuscular junction although they do not always improve the patient to the extent attainable by a spontaneous remission.

Edrophonium chloride (Tensilon®) (29, 30) is of no value in treatment. It is employed only as a diagnostic test or used in the mangement of the above three drugs in the treatment of the myasthenic patient.

It is generally accepted that the therapeutic efficacy of anticholinesterases is due to their inhibitory effect on the cholinesterase at the neuromuscular junction. The inhibition of this enzyme presumably causes accumulation of acetylcholine and this in turn results in the partial correction of the transmission defect (36).

Neostigmine bromide. 1) Neostigmine is effective in the treatment of the majority of cases; the milder type is particularly well controlled on relatively small dosages. 2) Neostigmine has withstood the test of time having been in use for over thirty-five years. It is not habit forming, since requirement for the drug diminishes as patients improve. 3) The disadvantages of neostigmine are that: (a) the drug has a short duration of action; (b) muscarinic side-effects such as epigastric distress, sweating, salivation, lacrimation, nausea, abdominal cramps, and diarrhea are pronounced and at times difficult to control despite the use of atropine; muscle fasciculations may occur. 4) Dosage of neostigmine varies from as little as one-half of one 15 mg tablet three times daily in mild cases to over 100 tablets (rare) per day in severe cases, although the required dosage seldom exceeds 10 tablets daily. It is usually prescribed every two to three hours. Menstrual periods, infection, or emotional stress can alter the daily requirement. The patient, with the help of his physician, must learn to adjust the dose to his immediate needs. Adjustment is based on the degree of relief of myasthenic symptomatology and upon the side-reactions which indicate that overdosage possibly leading to cholinergic reaction is being approached. The dose of any cholinergic drug should be increased slowly.

When the patient cannot swallow, neostigmine is available as a methylsulfate for parenteral use. An intravenous dosage of 0.5 mg is equivalent to 1.0–1.5 mg intramuscularly or 15.0 mg orally. Ampules of 1:4000 yielding 0.25 mg per ml; ampules of 1:2000 yielding 0.5 mg per ml; and 10 ml vials of 1:1000 yielding 1 mg per ml are obtainable.

Pyridostigmine bromide. Pyridostigmine is an analogue of neostigmine. 1) Its duration of action during the day is perhaps one-half-hour longer than that of neostigmine. In most patients the nocturnal relief with pyridostigmine is one of the most important advantages. No dosage is required during the night and even most patients with dysphagia arise in the morning able to swallow the first dose of the day. 2) Pyridostigmine is more effective than neostigmine in the relief of myasthenic symptoms affecting the small muscles innervated by the cranial nerves, particularly the muscles involved in ptosis, diplopia and dysarthria. 3) A striking advantage of pyridostigmine as compared to neostigmine is the low incidence of muscarinic side-effects such as epigastric distress, abdominal cramps and diarrhea, and the reduction of nicotinic side-effects such as skeletal muscle cramps. Atropine can be discontinued in 75 percent of patients who required it with neostigmine. Atropine should not be used routinely because it masks the early warning signs of approaching overdosage. Because the range between therapeutic and toxic levels of pyridostigmine is much greater than that of neostigmine no difficulty is encountered. The usual muscarinic side-reactions occur as soon as overdosage with pyridostigmine is reached. 4) A disadvantage of pyridostigmine is that some patients complain that they do not get the "lift" attainable with neostigmine. Most patients receiving pyridostigmine are satisfied with the general feeling of well-being during the day. 5) Dosage: The pyridostigmine bromide quarter-scored 60 mg tablet is equivalent to one 15 mg of the neostigmine bromide tablet. It is generally replaceable, tablet for tablet, with neostigmine and is given every three to four hours in most cases. In less than one percent of patients who develop bromidism, a 50 mg tablet of pyridostigmine chloride may be used. Pyridostigmine bromide is available from the manufacturer in 2 ml ampules containing 5 mg per ml for parenteral use. Whether given intravenously or intramuscularly, the dose of 2 mg is equivalent to a one 60 mg tablet of the regular pyridostigmine. Syrup of pyridostigmine yielding 12 mg to the ml or 1 teaspoon of 5 ml equal to one tablet is available and is particularly helpful in the pediatric myasthenic. It is also of great value in the patient with marked dysphagia and can be administered through a nasogastric tube when required. The apparent greater ease of absorption of the syrup vehicle may necessitate some reduction in total administered dosage.

Prolonged-action drugs. A preparation of pyridostigmine has been produced in which the drug is absorbed onto an inert base. Timespan® pyridostigmine tablets (46) contain 180 mg of pyridostigmine, and about one-third is released for immediate therapy giving the effect of one 60 mg regular pyridostigmine tablet. The remaining pyridostigmine is slowly released and its duration of action is 2 to 2½ times that of the regular 60 mg tablet. This is useful for the patient who would otherwise have to be awakened from sleep to take medication in order to prevent symptoms upon waking in the morning. However, dosage is reduced by ½ to 1 tablet because of diminished activity during sleep. It is rarely advisable to use this preparation during the day in patients who take large amounts of the drug because release and absorption of the active agent may be unpredictable and because it allows less flexibility than standard preparations.

In addition to the Timespan® mentioned above, over the years many drugs have been studied in an effort to decrease the need for frequent administration of the commonly short-acting drugs. Thus, organic phosphate compounds (47, 48), BC-51 (49), and phospholine iodide (50) have been tried and have not met enthusiastic reception because of prolonged inhibition of cholinesterase, which made overdosage a frequent complication.

Ambenonium chloride. If pyridostigmine does not give satisfactory results after an adequate trial, ambenonium may be *cautiously* tried. Ambenonium is a bismolecule and is different in structure from neostigmine or pyridostigmine. 1) Ambenonium is definitely longer in action than neostigmine and possibly slightly longer than pyridostigmine in the daytime hours but has the same nocturnal effect as regular pyridostigmine. 2) It has an excellent effect on the peripheral muscles affected by myasthenia gravis and gives a more sustained increase in strength. Its value for bulbar myasthenia is midway between that of pyridostigmine and neostigmine. 3) It has fewer toxic side-effects than neostigmine but more than pyridostigmine. These side-effects differ from those of pyridostigmine. Central nervous system side-effects are more evident, particularly headaches. Other early signs of overdosage are muscle fasciculations and weakness. Gastrointestinal side-reactions are not as common as with the other two drugs but do occur late when overdosage is approached. Ambenonium has a distinct advantage for the patient in crisis being treated with respiratory assistance, since it induces less bronchial secretions than other anticholinesterase drugs. 4) Dosage: Ambenonium is available in one-half scored 10 and 25 mg tablets. Approximately 6 mg of ambenonium chloride is equivalent to 15 mg of neostigmine bromide or 60 mg of pyridostigmine bromide. Ambenonium should be started *cautiously* with a 5 mg dose and gradually increased to therapeutic levels. It is usually prescribed every four hours. Ambenonium has a greater tendency towards prolongation and accumulation of drug effect towards the end of a day, requiring both dosage and periodicity adjustments in many patients.

This drug is also potentiated almost 100-fold, weight-for-weight, by the simultaneous administration of phospholine iodide, a long-term esterase inhibitor. This latter drug, occasionally used in ocular myasthenia and widely used in glaucoma therapy, contraindicates the coincident administration of ambenonium (50).

Despite the above mentioned differences in the three anticholinesterase drugs, in most patients the efficacy of each is about the same. Most patients prefer pyridostigmine because of decreased disagreeable intestinal side-reactions and its more sustained effect of strength between doses. If a patient is not doing well on one drug, the physician should prescribe one of the other drugs in an attempt to achieve better control. The better control so achieved is frequently more psychologic than real. Combinations of two drugs occasionally are better than the use of a single drug alone but generally have fallen into disuse in recent years.

The dosage of drug used varies from patient to patient and indeed may vary in the same patient with time of day and activity. Ordinarily the initial dosage may be 30 to 60 mg of pyridostigmine; 7.5 to 15 mg of neostigmine; 2.5 to 5 mg of ambenonium. The dosage is given three or sometimes four times a day. The dosage is increased gradually until maximum benefit is obtained with minimal side-reactions.

When anticholinesterase drugs are taken on an empty stomach their absorption is more rapid and may lead to some cholinergic effects. Therefore, it is advisable that the patient take medication after eating. For a patient who has dysphagia it is most important that the drug be administered with milk from one-half to one hour prior to a meal.

After determination of the optimal dosage of anticholinesterase drug, the most sutiable time interval between the administration of maintenance doses can be determined by observing the duration of the effect of medication. In general, readministration of the drug should be administered 60 to 90 minutes before the patient's condition returns to the basal state. This time interval is required before the next dose becomes effective. The usual time interval between doses of neostigmine are 2 to 4 hours and between those of pyridostigmine or ambenonium 3 to 6 hours. Many patients, however, require medication at considerable shorter, longer or variable intervals. Most patients do not require medication during the hours of sleep. Some, however, need anticholinesterase medication at regular intervals during the night. In most of these, the anticholinesterase drug requirements can be satisfied without the interruption of sleep by the administration of one or more 180 mg Timespan® pyridostigmine tablets.

Management edrophonium test. In the drug management of a myasthenic patient, use of empiric dosages by means of clinical judgment is frequently resorted to. It is most important to estimate how the patient feels one hour after taking his oral medication, for this is the time of optimal absorption from the gastrointestinal tract. If the patient feels improved as compared to just prior to drug taking and has minimal muscarinic side-reactions, but is not satisfied with the results of therapy, he is probably underdosed. With caution, small increases of anticholinesterase drug may be prescribed. If on the other hand, at this time interval, i.e., one hour, the patient feels worse than before taking his drug (with or without muscarinic side-reactions, but especially with them), there is fairly clear indication that overdosage or cholinergic effect is present. It is best to reduce dosage at this time and certainly to withhold another dose for a minimal period of at least one hour. Atropine may be prescribed to ablate muscarinic side-reactions. A third possibility is that one hour after taking medication the patient is feeling excellent, therefore, obviously he is adequately regulated. The above findings can be confirmed by resorting to a management edrophonium test (30). This test is again done at the one hour interval following oral dosage and the amount of edrophonium used is 2 mg intravenously. With this small amount there is little interference in reaction caused by edrophonium. Effects seen clearly delineate a response based on the oral drug administered one hour earlier. Other investigators have recommended dosage

TABLE III

Approximate Equivalent Doses of Commonly Used Anticholinesterases

Drug	Oral Dose	Intravenous Dose	Intramuscular
Neostigmine (Prostigmin®)	15 mg	0.5 mg	1–1.5 mg
Pyridostigmine (Mestinon®)	60 mg	2.0 mg	2.0 mg
Pyridostigmine Syrup	60 mg/5 ml		
Pyridostigmine (Timespan®)	180 mg		
Pyridostigmine Chloride	50 mg		
Ambenonium (Mytelase)®	5–7.5 mg	none available	none available

variations of 3, 4, and even 10 mg. With these higher dosages, at times one may see improvement of symptoms which are not evident after the use of 0.2 ml (2.0 mg). More often, one may see an effect in which certain areas of muscle weakness are improved while other striated muscles become weaker. This makes it difficult to interpret the test. Occasionally, one can observe such a dichotomy of results even when using only 0.2 ml. (2.0 mg.). When at times diplopia becomes more severe, yet ptosis lessens, the more disabling symptom should be considered more important. Only in rare instances does increasing the edrophonium test to 4 or 5 mg give additional information.

In some myasthenic patients it is important to compare the management edrophonium test with results of a placebo injection. However, some myasthenic patients quickly learn to evaluate effects of edrophonium as compared to a saline placebo. This may be obviated by using nicotinic acid or calcium as the placebo.

The edrophonium test can be used to determine frequency of oral anticholinesterase medication. This is not important in the easily controlled patient. In the difficult patient, especially the seriously ill myasthenic, edrophonium testing should be done at the end of a dose period in order to avoid administration of oral medication before the patient demonstrates a clear myasthenic response. Only when good improvement is observed following testing, should another oral dose of anticholinesterase drug be given. This avoids development of a cholinergic reaction which might be caused by the giving of treatment drug at set intervals. Avoidance of drug accumulation is thus achieved. Administration of each successive dose, once stable response is obtained, will then generally anticipate the point of maximum edrophonium response by one-half to three-quarters of an hour.

How frequently should the edrophonium test be performed in order to determine drug dosage? In earlier experimental stages, testing was done at hourly intervals. At present, for the hospitalized patient admitted for regulation, testing for adequacy of dosage on a daily basis, or even every two to three days, imparts sufficient information. It usually takes a day or two for changes in oral medication to show their full effect. It is also advisable to test differently timed oral dosages as there may be variations in amounts required at different times during the day. If edrophonium tests are performed too frequently, there is a tendency to adjust oral medication too often, thus possibly building towards a cholinergic response. In the hospitalized, "brittle" myasthenic, frequently repeated edrophonium tests, even with low dosages, may provoke cholinergic reactions including prolonged nicotinic ganglionic block. In such cases, repeated tests should not be done for several hours. The term "brittle myasthenia" is applied when the patient alternates rapidly between myasthenic and cholinergic states. There is an inconstant response to medication for days to weeks without rapid progression to acute respiratory insufficiency. For the ambulatory patient, testing can be utilized to verify the clinical response of the patient since his last visit, as well as to explain subjective symptomatology related to anticholinesterase drugs.

ADJUVANT DRUGS

The anticholinesterases used in the treatment of myasthenia gravis do possess potent muscarinic effects as indicated by their pharmacologic nature. These effects do not necessarily manifest themselves only at toxic levels, but rather depending on individual sensitivity, may be present at therapeutic or below therapeutic dosages necessary. The ablation of such side-effects is therefore mandatory in many instances albeit that such ablation may mask the beginning of significant toxicity.

Atropine sulfate (40) and propantheline (Probanthine®) (36) are commonly used agents. Atropine 0.4 to 1.0 mg. orally, intramuscularly or intravenously may be administered to relieve excessive salivation, diaphoresis, abdominal cramps, diarrhea, hyperacidity, ulcer pain and other muscarinic side-effects. Bronchorrhea may be especially troublesome, yet overtreatment with atropine may result in inspissated secretions and atelectasis so that tracheobronchial toilette is crucial (51).

After optimal control with anticholinesterase drugs has been achieved, there still may be a marked clinical deficit for the myasthenic patient. In such events resort to adjuvant drugs has been advocated. These drugs include ephedrine (52), potassium (53), potassium-sparing drugs such as spironolactone (Aldactone®) (54), triameterene (Dyrenium®) (55), and more recently calcium (56). In most instances these adjuvants have little use, but an occasional patient will be benefited. There is no reason for a patient to take any of these adjuvant medications unless there is clear clinical evidence that they are helpful, i.e., a ptosis which is incompletely relieved with pyridostigmine is completely relieved with pyridostigmine and the addition of ephedrine.

Ephedrine sulfate dosage is 25 mg three times a day. In the elderly male this may cause micturition problems and if this occurs ephedrine should be stopped. Potassium is administered in liquid form 15 30 mEq three times a day after meals. Spironolactone is prescribed in 25 mg doses four times a day. Triameterene is taken as a 100 mg capsule 2 to 3 times a day. One does not use these two drugs together, but one or the other, and serum potassium levels should be monitored. Calcium is given as gluconate 1 gram orally four times a day.

When prescribing adjuvants, the patient should be given a one-week trial with one of the above. If ineffective, discontinue and resort to another adjuvant. If effective, they can be continued until benefit is lost. After a few weeks rest, one can restart to see if the drug improves clinical response.

Under investigation and clinical evaluation at the present time is a veratrum derivative, germine monoacetate. This drug potentiates repetitive muscle response to minimal and apparently deficient neurogenic stimuli. Its action is thus entirely different, yet apparently additive to the anticholinesterase effect. The demonstrated capability makes this drug the first true and distinct adjuvant drug available. Supplies are short and synthesis is difficult so that these conclusions still represent only limited pilot studies (57).

Other therapeutic drugs. In 1948 adrenocorticotrophic hormone (ACTH) was administered in order to shrink thymoma (58). Subsequently it was used as a means of medical thymectomy (59) but fell into disregard because it was potentially hazardous in that during the early stages of its administration, the patient's disease was exacerbated and death ensued from respiratory arrest (60). In 1965 this drug was reinvestigated and found to be of great value in the treatment of severe myasthenics (Groups III and IV) (61). The new method of administration included admission to an Intensive Care Unit and elective tracheostomy performed prior to using ACTH. Thus, the marked exacerbation of symptomatology during the course of treatment can be controlled by assisted respiration which is required in almost 80 percent of patients (62, 63). In some institutions where intubation can be quickly performed, tracheostomy is delayed until necessary. However, in our opinion, pretreatment tracheostomy should be required before initiatiating ACTH therapy.

ACTH is administered in a course of 100 units of gel intramuscularly daily for ten days. Anticholinesterase medication is not discontinued because its withdrawal creates myasthenic weakness and with the weakness induced by ACTH makes a patient so limp that he becomes a major nursing problem (64). In most instances we reduce the anticholinesterase drug by one-fourth to one-third and continue it throughout the ten-day course. When dysphagia supervenes, gavage feedings through a nasogastric tube are started and the anticholinesterase drug is changed to syrup of pyridostigmine. When the patient is on Timespan® pyridostigmine for the last dose of the day, the dosage is converted to syrup and is given during the night, at appropriate intervals.

ACTH should not be prescribed for patients with known peptic ulcers since bleeding may be induced. Thus, all patients should have stool guaiacs, daily hemoglobins, and hematocrits to observe for possible gastrointestinal bleeding. Electrolyte studies, blood chemistries, and humoral and cellular antibody titers are performed every second or third day.

At the end of the tenth day of treatment, ACTH injections are abruptly stopped. No attempt to change anticholinesterase drug treatment is made until three to four days following cessation of ACTH, at which time the patient should begin to show clinical improvement; and adjustment of specific drugs can be attempted by resorting to the edrophonium test.

Improvement will occur in over 90 percent of patients, some even without showing clinical weakness during the course, although such weakness is usually directly proportional to the improvement noted. The effects of ACTH treatment are usually not permanent and may require reinstitution as early as three months following discharge from the hospital. This is particularly true of the very severely ill myasthenic patient and especially true of those who have had thymectomy for removal of thymoma. When no or insufficient improvement is noted by the seventh day following an ACTH course, a second "paired" ten-day course should be administered. This often results in the desired clinical improvement. A major residual deficit may even respond to a third "paired" course (62). Such additional ACTH administration should not be delayed more than seven days as it has been noted empirically that additive effects will not be attained with greater delay. There is no benefit and indeed some increased danger to the prolongation of any one course beyond the ten-day limit.

A cooperative study has administered some 300 courses of ACTH to 100 patients, male and female, young and old, with or without thymoma, pre- and postthymectomy. The study included patients who had "brittle," refractory, and severe myasthenia gravis. This group included a small but significant number of patients who previously made up the bulk of patient hospital days (65). This modality permitted a return to functional life previously unreachable.

The premorbid psychiatric state of the patient, particularly in the older age range, must be evaluated because of ACTH enhancement of pretreatment psychosis. Though this mental state may be severe, it is usually brief in duration. Its occurrence is rare but dramatic.

ACTH has also been used as an interval treatment of a single injection (100 U) administration at weekly, biweekly and triweekly periods. In selected patients prolongation between courses has been achieved and an occasional patient has been maintained in remission with such therapy alone (65, 66). The severe weakness occasionally encountered after a single injection, makes patient selection critical and mandates continued tracheostomy with availability of respiratory assistance at home.

Besides the gastrointestinal hemorrhages previously mentioned, a second major complication in ACTH therapy is that of masked and refractory infection, especially of a pulmonary nature, with overgrowth of unusually resistant organisms. This must be carefully watched for and if infection is present, it should be controlled prior to ACTH therapy. If infection is intercurrent, treatment may have to be discontinued.

When other diseases in a myasthenic patient commonly treated with ACTH are encountered, such as systemic lupus erythematosus, pemphigus vulgaris, bronchial asthma, hemolytic anemia, and rheumatoid arthritis, the ACTH effect may cause initial exacerbation of myasthenic symptoms. A more restricted experience is under evaluation employing prednisolone, orally, in doses of 40 to 60 mg daily in divided doses (67). There is even some early study of maintenance therapy with daily oral doses of prednisolone of 5 to 15 mg. While some investigators report results similar to ACTH, our own data are not favorable. We have noted less and shorter-lasting improvement and an apparent greater increase of "steroid" complications. Recent reports of alternate-day high dosage (100 mg) with oral prednisone is most challenging since marked benefits have been seen (68). Again more extensive experience with slightly lower dosage at our institution has not borne this out, however, reassessment is under study.

Immunosuppressive drugs. These drugs have not yet received adequate clinical trial. The theoretical basis for their use is discussed in the second section of this review. Spurred by the autoimmune concept of myasthenia gravis (69, 11), and prior to the reaffirmation of the value of ACTH, investigators tried immunosuppressive agents on an empiric basis. Because of the hazards of such therapy, quantitative controls and total protocols have varied widely in the total experience of less than 100 cases in the world literature (70). Dosage endpoint and deviation of courses have been uneven. The agents used have included 6-mercaptopurine, aziothioprine (Immuran®), and cyclophosphomide

(Cytoxan®) and methotrexate. Results are most inconclusive, yet occasionally have been favorable (71). Complications are frequent.

The more recent cellular immunity concepts indicate a full clinical trial with antilymphocytic and antithymocytic globulins. This will serve as an important therapeutic test and investigative tool. The experience derived from transplantation surgery and use of these agents in documented autoimmune diseases is being studied prior to application of a standard protocol (72).

CONTRAINDICATED DRUGS

Numerous drugs are known to effect neuromuscular transmission. The action of some of these may seriously potentiate the myasthenic deficit and should be avoided whenever possible or should be used with awareness and caution. When other overriding medical indications mandate administration of such drugs, this awareness may be critical (36).

A partial listing of commonly used drugs in this category includes the following.

Quinine and quinidine. These compounds inhibit neuromuscular transmission (73), probably by interfering with the spread of excitation along the muscle fiber (74). They will increase the muscle weakness in myasthenia gravis (75) and whenever possible their use should be avoided. The amount of quinine present in a glass of tonic water may cause difficulties in myasthenic subjects.

Procainamide. This compound administered to control ventricular arrhythmia in a myasthenic subject, consistently increased muscle weakness (76). Consequently, procainamide should be included in the list of drugs to be avoided in myasthenia gravis. There are no contraindications to the use of digitalis, lidocaine, or sodium diphenylhydantoin (Dilantin®) in cardiac arrhythmias in myasthenic patients.

Inhalation anesthetic agents. It has long been known that ether (77) has a depressant effect on neuromuscular transmission and that other inhalation anesthetic agents potentiate the action of d-tubocurarine and other nondepolarizing relaxants (78). Later reports (79, 80) revealed that although ether and other inhalation anesthetic agents (e.g., halothane, chloroform, trichloroethylene (Trilene®)) can cause muscular relaxation, the mechanism of their action is different from that of d-tubocurarine. Because of their effect on neuromuscular transmission, potent inhalation anesthetic agents should be used with extreme care in myasthenia gravis.

Barbiturates. Pentobarbital sodium (Nembutal®), secobarbital sodium (Seconal®), and phenobarbital sodium (Luminal®) increase the neuromuscular blocking action of d-tubocurarine (81, 82). Large doses of barbiturates may have an adverse effect on neuromuscular transmission in myasthenia gravis.

Tranquilizers. Chlorpromazine intensifies the effects of d-tubocurarine and gallamine (83). Other tranquilizers (e.g. meprobamate) depress transmission of the nerve impulse in the spinal cord and thereby may cause further deterioration of muscle function in myasthenia gravis (84). Consequently great care should be exercised in the selection and administration of these compounds to myasthenic subjects. The nature of the myasthenic syndrome is such that for many patients the use of tranquilizers is essential. Awareness of such potential effects becomes doubly important.

Antibiotics. Many antibotics such as streptomycin and neomycin have a weak neuromuscular blocking effect. They may potentiate the effect of nondepolarizing block. After prolonged administration they may potentiate a depolarizing block. Increased muscle weakness has been reported after the administration of streptomycin or dihydrostreptomycin to myasthenic subjects. In addition neomycin, viomycin, kanamycin, colistin, polymycin A and B, paromomycin, tetracycline and sulfonamides may have a similar effect in myasthenia gravis (85). Frequent and severe respiratory infections of myasthenic patients mandate the use of antibiotics with care.

Ganglionic blocking agents. Several ganglionic blocking agents such as guanethidine (Ismelin®), hexamethonium, homatropinium (Trophenium®), and mecamylamine potentiate the effect of d-tubocurarine and may adversely effect neuromuscular transmission in myasthenia gravis.

Diuretics. The potassium depleting effect of the administration of many diuretics with resultant neuromuscular and depolarizing blocks must also be considered. The specific potassium sparing actions of spironolactone and triamterene have been employed as adjuvant drugs with some benefit.

The Thymus and Myasthenia Gravis

The paucity of pathology in postmortem examinations and the confusion of "thymic" pathology did not permit much more than a statement of a statistical fact for many years. Fundamental light microscopic and gross pathologic classifications by Castleman (86) and newer histochemical and embryologic insights have clarified the issue over the past two decades (87). The present status has been further refined by the thrust of basic work by Burnet (88) and others linking the thymus to autoimmune disease.

The following pathologic facts are accepted today:

1. When the age of patients is considered, 65 to 70 percent of myasthenic patients have demonstrable thymic abnormalities (89). Such pathology varies from "persistent" or "hyperplastic" thymuses to actual thymoma formation or coexistence of the foregoing (90).

2. Persistence and hyperplasia of germinal centers in the thymus glands is found in numerous myasthenic patients (70 percent) (89).

Structurally, the thymus consists of two types of cells, epithelial and lymphoid components, very variable in composition (91). The lymphoid aggregates in germinal centers and the entire gland normally atrophies by the middle of the second decade of life. In the myasthenic, with the exception of a small number of older patients, we have not failed to find a structurally distinct, anatomically identifiable thymus. The term hyperplastic is somewhat unfortunate and the term "persistent" is perhaps better. There is a paucity of data, particularly in the line of sophisticated serial x-ray studies to document regrowth, persistence, or enlargement of thymus through the teens. Posterior-anterior chest films are quite inadequate for answers. When regarded as a malignant tumor, the thymoma itself fails to meet pathologic criteria for this label. There are no nuclear anomalies, including mitosis. While the lymphoid portion of thymomas and persistent glands are histologically indistinguishable, the epithelial cells are more characteristic. Initial interest in "myoid" cells has waned and spindle cells alone do not appear associated with myasthenia gravis as they are with aregenerative erythroid crisis. A plump, extremely radioresistant type of epithelial cell, often glycogen-containing, is an almost invariable constant (91). Recent interest in germinal centers and autoimmune disease may perhaps have shifted deserved interest away from these cells and their tissue culture study.

Metastases by other than direct extension are quite unknown without previous surgical manipulation which may technically cause hematologic or lymphogenic dissemination. If one uses the criterion of breakthrough of capsules and involvement of contiguous structures, then fully 80 percent of thymomas are malignant (91).

To date serial study by x-ray to verify findings regarding correlative growth and tumorfaction of the thymus in the myasthenic has not been fruitful. Thus, newer techniques of sectional radiography, angiography (92), and isotope scanning (93) applied on a wider basis and in a serial study may be most useful. Thymectomy has not been performed in Group I and only modestly in Group IIA patients. Therefore, there is little data regarding thymic structure in these numerically important groups.

Antibody studies may also help in selection of patients for more than routine x-ray in that sudden increase of titer or the development of a positive from a previously negative titer may make such a search rewarding in discovering thymoma (94–96).

Why then thymectomy in myasthenia gravis?

THYMECTOMY

Surgical removal of the thymus gland has been the logical result of the association of thymic pathology and myasthenia gravis. Favorable early reports on results of thymectomy (97) were tempered by later less enthusiastic analyses (98). The major difficulties were lack of unified patient selection and classification, different modes of surgery and particularly a lack of unified operative and postoperative patient management. Awareness of these factors makes mandatory the division of patients into groups with and without tumor (99). Recently, indications for thymectomy have been liberalized.

Careful attention to detail in preoperative preparation, anesthetic management and postoperative care (90, 100) have markedly reduced mortality and morbidity in thymectomy. Obligatory tracheostomy, mechanically controlled or assisted ventilation, and the withdrawal of anticholinesterase medication in the immediate postoperative period are essential features in management of the myasthenia gravis patient undergoing thymectomy. Postoperatively, it is also important to place thymectomized patients in an Intensive Care Unit where specially trained personnel are available on a twenty-four hour basis.

From 1939 to 1965 there was no clear indication as to whom should be a candidate for thymectomy. In fact, under the aegis of the National Institutes of Health, a projective study was contemplated in order to solve this problem. Because of multiple difficulties regarding controls, financing, homogenicity, surgical and postoperative techniques, and since there was a large, well-documented patient population in two separate institutions, a different type of validation was accomplished, although retrospectively.

A cooperative study comparing survivorship and morbidity of 1,355 myasthenia gravis patients has been carried out by the Myasthenia Gravis Clinics of Massachusetts General Hospital, Boston, and The Mount Sinai Hospital, New York City (20). This study evaluated relative effectiveness of medical and surgical therapy.

Patients in each institution were surveyed to determine eligibility for admission in this study. Pertinent data concerning each patient from onset of disease to the most recent evaluation or death were processed separately by each institution and information was coded in a uniform manner on IBM cards. Information included sex, race, age at onset, type and severity of myasthenia gravis at onset, and, at time of last follow-up examination, type of treatment, result of treatment, duration of illness, cause of death, and presence or absence of thymoma.

This study analyzed 1,355 patients with myasthenia gravis. Of the total patients, 723 were registered at The Mount Sinai Hospital and 632 at Massachusetts General Hospital.

One hundred and eighty-eight patients without thymoma were treated by thymectomy. Duration of myasthenia from onset to operation varied considerably. In only 7 percent of patients, duration was less than one year; in 63 percent, one to six years; in 21 percent, six to twelve years; and in only 9 percent, twelve to twenty-three years. Of the 188 patients, 144 were alive and evaluated in 1965. Striking benefit from thymectomy was shown for females, with a 38 percent total remission rate and 51 percent improvement, totaling 89 percent. Complete remission rate in nonoperated females was only 14 percent and an additional 18 percent were improved over the period of observation. Thymectomy in males also produced improvement in the remission rate, with 37 percent for those with thymectomy and 11 percent for those without. Surgical experience with males was relatively small; a total of 30 had thymectomy performed.

Operative mortality has steadily decreased with improvement in surgical techniques and postoperative management. During the past five years, operative mortality has been less than 2 percent.

In 1968 further interest in thymectomy was kindled by an article by Mackay et al (101) in a provocative report that suggested a rationale for thymectomy. They correlated results of thymectomy with autoimmune serologic tests, electromyographic changes, and thymic pathology. They suggested that the pathology in the thymus gland, namely thymic lymphoid follicular hyperplasia (germinal centers) may be a reflection of a distinctive autoimmune "thymitis" —analogous to the process seen in Hashimoto's thyroiditis leading to elaboration

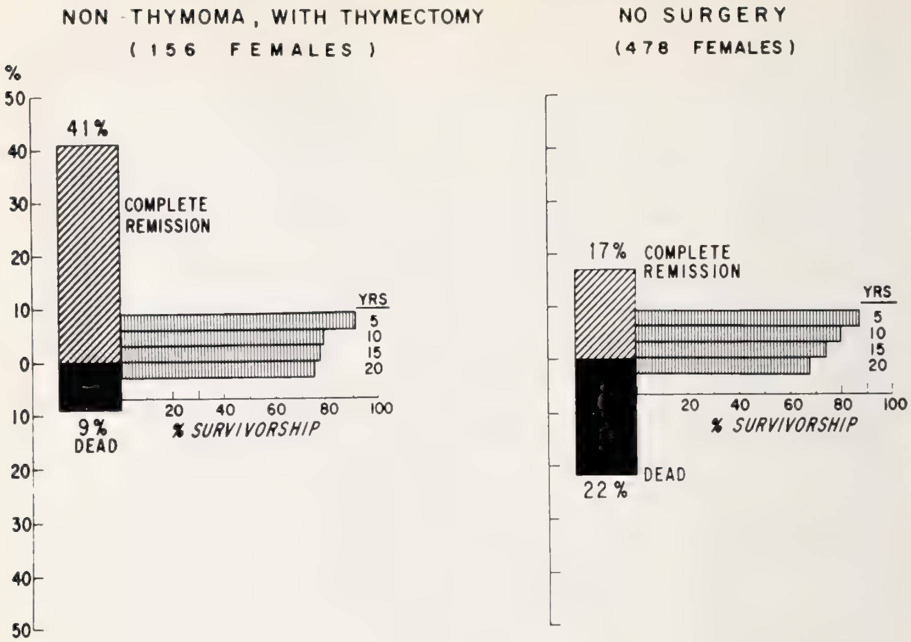

FIG. 3. Reprinted from Perlo et al. Permission granted by *Neurology* 16:431–39, 1966.

of a neuromuscular humoral blockading agent. Their study of a small series (10 cases) was subdivided into three groups. Groups A and C showed characteristic "thymitis," Group C being thymomas. These two groups showed marked improvement after thymectomy. Group B were females showing poor results from surgery in which thymic pathology predominantly demonstrated involution and atrophy. In an editorial for *The Annals of Internal Medicine*, Osserman concluded that confirmation of their findings would be important (102). Subsequently, a histologic reappraisal of myasthenia gravis was reported from our institution (89). In order to accomplish this it became advisable to reanalyze results of thymectomy at The Mount Sinai Hospital.

In 1967, we first started to perform thymectomy through a transcervical approach rather than the previously used sternal-splitting technique (103). Pathologic studies were performed without any knowledge of the results of surgery; which were compiled by another team who had no knowledge of the histologic appraisal of the thymus. When results of the study were finally correlated, it was noted that the sole histologic feature in distinguishing thymuses with myasthenia from those without myasthenia was appearance of medullary follicular hyperplasia in the former. This medullary follicular hyperplasia generally occurred in the non-neoplastic thymuses but not infrequently in the residual thymic tissue accompanying thymomas and occasionally within the thymomas itself (89).

Presence of thymic lymphoid follicles appeared to be unrelated to age, sex, duration of symptoms prior to surgery, clinical grouping at time of surgery or the presence of antibodies circulating to skeletal muscle. They were found, in our series, in approximately 75 percent of all non-neoplastic thymuses removed for the treatment of myasthenia gravis.

In the clinical appraisal, one thousand and two patients were followed by the Myasthenia Gravis Clinic of The Mount Sinai Hospital, of whom 185 (18.5 percent) underwent thymectomy between 1941 and 1969. One hundred and twenty-four patients were operated on at The Mount Sinai Hospital and 61 elsewhere (104).

Patients who underwent thymectomy were grouped into those with and without thymoma. The non-thymoma group consisted of 111 patients with generalized, respiratory, or late severe myasthenia gravis (Groups II, III, and IV of Clinical Classification).

The transcervical technique has been used since 1967 in all patients except those with inaccessible thymomas or low-lying preexisting tracheostomies (103). Of forty patients operated on through this approach, 28 were followed for six months and were included in the study. Since 1958, a routine tracheostomy has accompanied every thymectomy at our institution, a procedure that permits limitation of anticholinesterase drugs in the early postoperative period, thereby considerably lessening postoperative pulmonary complications (105).

In the first evaluation of results in this group, it was found that total remission rate was lower than that which had been reported in 1966 (20). The first concern was that 28 patients included in the 111 nonthymoma thymectomies were performed by this transcervical technique and that possibly there was incomplete resection of the thymus; therefore, this might be reducing the remission rate. In order to evaluate this possibility, it was decided to analyze remission rate at yearly intervals to determine whether it was transcervical thymectomies or the time interval following thymectomy which was important. As a result of this study, we found that the time interval following thymectomy was the important factor and not whether operation was transcervical or sternal-splitting. There was a gradual increase in the percentage of patients in remission with each increasing year following thymectomy up to a plateau that was reached about the seventh year.

Eighty-four of 111 patients (75 percent) were in remission or showed improvement. Percentage of male patients in remission (36 percent) was higher than that in female patients (22 percent). Of the 96 survivors, 87 percent were in remission or showed improvement. While 67 patients (60 percent) were in groups III and IV preoperatively, only three (2.7 percent) remained in these groups at time of evaluation. Sixteen female patients above the age of 30 had comparable results (81 percent remission and improvement). Patients with duration of symptoms of five years or more, showed a larger percentage in remission (26.4 percent) and a lower overall mortality (8.8 percent) when compared to those with duration of symptoms of less than five years prior to thymectomy (22 percent and 15.3 percent, respectively). This unusual finding was in contrast with most reports on the effectiveness of thymectomy in long standing myasthenia gravis (97, 98).

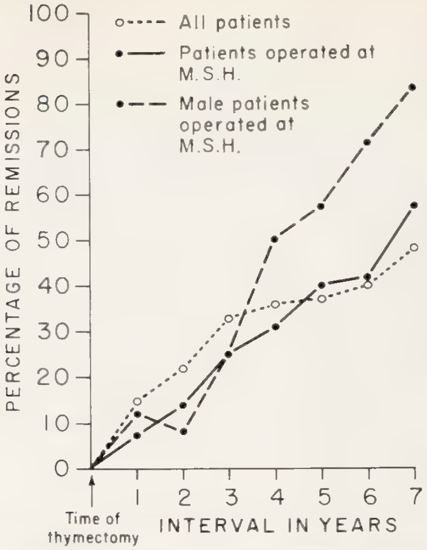

FIG. 4. Increasing remission rate in years following thymectomy. Reprinted from Papatestas et al., Permission granted by The American Journal of Medicine, 50:465–476, 1971.

When the code was broken between the pathologic studies and clinical evaluation, it was found that the presence or absence of germinal centers was apparently an important factor. Presence of germinal centers based on the number per low-powered field revealed that patients with absent or rare germinal centers (zero to one) had shorter intervals between thymectomy and onset of remission than those with numerous germinal centers (2 to 5+ per low-powered field).

Germinal centers in the surgical specimen were present in all patients who died and were only present in 66 percent of survivors. Figure 5 shows graphically the difference in time intervals in attaining remission, dependent upon presence or absence of germinal centers. This finding is in contrast to that which was reported by Mackay et al (101).

In order to verify the above noted results, namely that remission rate is a determinate of time postoperatively and the presence or absence of germinal centers, it was decided to ask our colleagues at Massachusetts General Hospital to analyze their series of thymectomies in a like manner. Therefore, for the Fourth International Myasthenia Gravis Conference a cooperative study of thymectomy was again undertaken by the Massachusetts General Hospital and The Mount Sinai Hospital (106). Two hundred and sixty-seven patients without thymoma were studied. Fifty were males and 217 females. One hundred and fifty-six were seen at Massachusetts General Hospital and 111 at our institution.

Figure 6 demonstrates the difference in time of onset of remission with the number of germinal centers present at time of operation. In the first four years following surgery, patients with zero to rare germinal centers had a high remis-

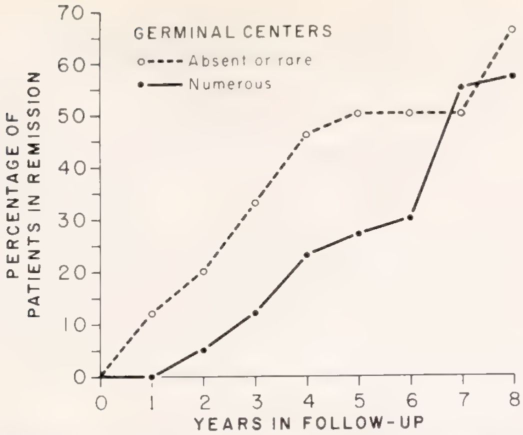

FIG. 5. Relationship of germinal centers to remission rate with time. Reprinted from Papatestas et al., Permission granted by The American Journal of Medicine, 50:465–476, 1971.

sion rate while those with many germinal centers showed a much reduced remission rate. At the end of one year patients with zero to rare germinal centers had a 45 percent remission rate compared with 12 percent of those with many germinal centers. The remission rates after two years were 61 percent compared with 32 percent; and at four years, 76 percent compared with 44 percent. The two curves began to approach each other beyond four years and met after the tenth year.

Thus, relationship between thymic germinal centers found at time of surgery and subsequent clinical course indicates the speed with which remission may take place. The number of germinal centers found at time of operation ceases to be significant as far as correlation with clinical results after a period of ten years following thymectomy (106).

As a result of the two cooperative studies with Massachusetts General Hospital and the recently reported study of effects of thymectomy from our institution, there is no question that the controversy that existed from 1940 to 1965 as to whether this procedure was a valid one has now been laid to rest. At this point in time, thymectomy is the accepted treatment for the severe myasthenic.

THYMOMA

The presence of a thymoma with myasthenia gravis has long been noted to herald a poor prognosis (99). Until a few years ago, indication for thymectomy for thymoma was an attempt to remove a malignant or possibly malignant tumor. At no time was any indication made that the myasthenia gravis itself could be ameliorated by operative intervention. The indication was simply to remove a potential malignancy.

Poorly understood is the association of myasthenia gravis with thymomas. The tumors appear to represent a relatively late stage in the progression of thymic pathology, earlier manifestations of which are hyperplasia and germinal

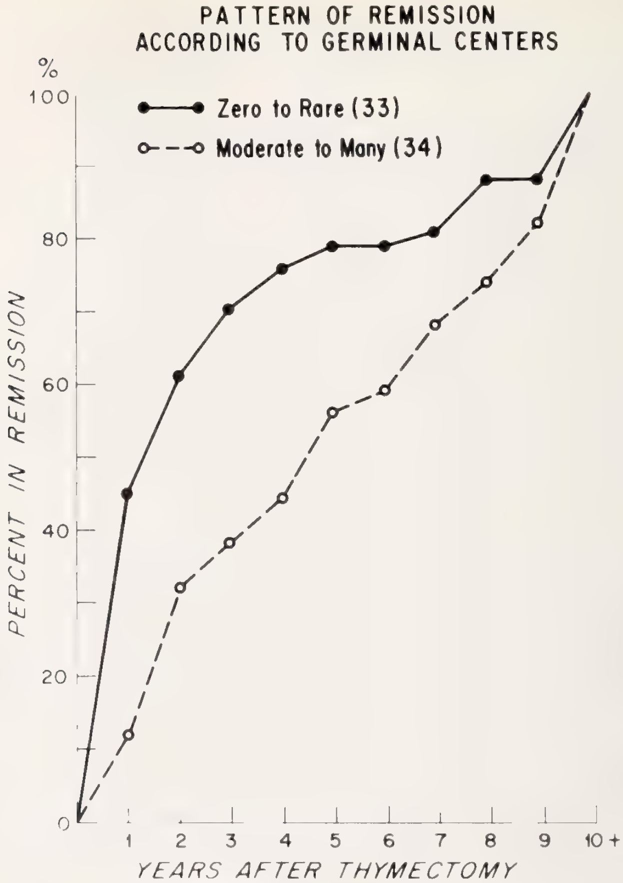

Fig. 6. Combined experience of Massachusetts General and The Mount Sinai Hospitals. Reprinted from Perlo, et al. Permission granted by The Annals of the New York Academy of Sciences. In press.

follicle formation (107). Castleman (86) found that 10 percent of patients with myasthenia gravis have thymomas. Keynes (108) reported an incidence of 15.4 percent of thymomas in patients subjected to thymectomy.

Often thymomas associated with myasthenia gravis are locally invasive tumors. Though histologically benign, they may behave it a malignant manner by invading adjacent structures. Rate of invasiveness varies among different series and figures as high as 80 percent have been reported (91). Mortality rate of 70 percent has been reported in patients with radiologic evidence of thymoma, whereas, mortality rate of 40 percent has been found in those without radiologic evidence of mediastinal tumor (109). In our group, all the patients who died had evidence of a tumor mass on their preoperative chest x-ray. In our institution the incidence of thymoma among all myasthenic patients has been 11 percent.

Invasive thymomas were found in 20 of 45 patients operated upon and intrathoracic metastases were present in three. Five of eight patients who developed myasthenia following thymectomy were found to have malignant thymomas at operation. Based on reports from the literature, it would seem that residual thymus or tumor is one of the causes for the persistence of myasthenic symptoms after thymectomy or for appearance of the disease postthymectomy (18, 110–112).

Deaths occurring after the fourth postoperative year occurred only among patients with invasive thymomas. In a report of 60 thymic tumors, it was noted that deaths after four years occurred only in malignant thymomas (113).

Thymectomy without excision of the residual thymus as performed in several centers should not be considered as adequate even in the absence of myasthenia gravis, since residual thymus may cause postoperative appearance of the disease (113).

Since residual thymus was not available for pathologic examination in all specimens of thymoma removed, no correlation between germinal centers and clinical course was attempted because of the lower percentage of patients with germinal centers in the thymoma group.

In our *American Journal of Medicine* report of thymectomy in myasthenia gravis (104), 6.5 percent of patients with thymoma were in remission and 18.6 percent demonstrated improvement. Myasthenic deaths occurring five years or more after thymectomy were found only in those patients exhibiting invasive tumors. When the patient survived two years postoperatively, 33 percent of males and 13 percent of females were in remission.

Thus, we can now state that indications for thymectomy in a myasthenic patient with thymoma are not only to remove a potentially malignant tumor, but also to help ameliorate the devastating course of the disease.

RADIATION THERAPY

Radiation therapy applied to the anterior mediastinum has been recommended in the treatment of myasthenia gravis both in the absence (114, 115) and in the presence of thymomas (116) alone or in conjunction with surgery (108). Recommended doses were 600 to 2000 R (114, 115) and 4000 to 6000 R (108) respectively in the absence or presence of thymoma. Radiation therapy

TABLE IV

Indications for Thymectomy

I. Nonthymoma Cases
    A. Groups IIB, III and IV.
        1. Both sexes
        2. Age group 6–60 years with emphasis on the 15–45 year old patients.
        3. Myasthenic patients uncontrollable with anticholinesterase medications.
    B. A selective study is now in progress in Group IIA patients.
        It is still considered desirable to operate early.
II. Thymoma Cases
        All patients if good surgical risk.

primarily affects the lymphoid elements of thymic tissue and has little effect on the epithelioid cells (91).

Radiation therapy must be administered slowly, with gradually increasing doses over relatively long periods. Even with these precautions, exacerbations associated with cholinergic manifestations may be encountered during treatment.

Radiotherapy in prethymectomy patients demonstrates a reduction to total absence of germinal centers and other thymic lymphoid elements (106). Preoperative application of radiotherapy to patients, thus, may logically be expected to shorten the observed lag before significant symptomatic improvement. It may further shed light on the relationship between the presence of these lymphoid structures and the subsequent clinical course of the patient.

In the absence of an adequate, statistically analyzed series, it is difficult to evaluate the usefulness of radiation therapy. Such evaluation is further hampered by the results of radiation obtained with earlier ("grid") techniques and are not comparable to those of the presently used "teletherapy" and "supervoltage" techniques. With the increased safety and well-documented efficacy of thymectomy (20), the use of radiation therapy should be restricted, at present, to those exceptional cases where surgery is contraindicated on other medical grounds (36).

Crisis and Its Management

In the course of myasthenia gravis, the most dramatic and critical event is that of crisis. Whether "myasthenic" crisis (severe weakness caused by insufficient drugs to cope with acceleration of disease) or whether "cholinergic" crisis (nicotinic ganglionic blockade caused by anticholinesterase overdosage) has occurred, respiratory insufficiency is the common denominator. This respiratory failure is a multiple phenomenon. Hypoventilation, poor gas exchange, muscle weakness of intercostals and diaphragm, accumulation of secretions and inability to clear them, atelectasis, and infection each add to this pyramid.

The end result is that of total cardiorespiratory collapse and death. As these contributory points are mentioned, sequence and priority of their repair suggests themselves. Operative intervention, i.e. thymectomy, adds its own burden, particularly if the sternal-splitting technique is employed (103).

The first step is then one of recognition of type of crisis. Pathophysiology of crisis is divisible into three categories:

MYASTHENIC CRISIS

Patients with severe generalized myasthenia gravis, Clinical Groups IIB, III and IV may have acceleration of disease either sui generis, or caused by intercurrent infection, emotional trauma, or other complications. There may be progressive inability to swallow resulting in inadequate ingestion of medication leading to involvement of respiratory muscles in the myasthenic competitive curare-like block. Onset may be insidious, contributing to a critical state where the combination of factors previously mentioned results in respiratory failure. If the physician is clear about such facts, then administration of parenteral anticholinesterase agents often promptly reverses the process. This depends, in large measure, on how far this situation has developed. (See Table V.)

CHOLINERGIC CRISIS

As with many other disease entities requiring maintenance therapy, alterations by the patient or spontaneous reduction in drug requirement may occur. Drug accumulation, particularly with ambenonium is also possible. While adequate amounts of cholinergic drugs are mandatory, overdosage, however arrived at, creates serious problems. Nicotinic ganglionic blockade (depolarizing block) may then occur, leading again to the same respiratory failure.

BRITTLE CRISIS.

In instances of severe clinical bulbar involvement, particularly associated with thymoma, there may develop in the course of therapy a type of insensitive block with unpredictable inversions of the therapeutic index for anticholinesterase drugs. In these patients there are rapid and irregular alternations of "cholinergic" and "myasthenic" states culminating again in respiratory failure. In this brittle state, clinical response to both edrophonium testing and anticholinesterase drugs is inconsistent and difficult to evaluate (51).

Each of the foregoing types of crises presumes preexisting clinical awareness of the presence of myasthenia gravis in the patient. Myasthenic crisis may, however, supervene without such information particularly at time of anesthesia, or with administration of quinidine or with other drugs in a patient in whom this disease had not been recognized previously.

At first, crisis was considered to be present only when the patient stopped breathing. With increasing experience, earlier phases of respiratory distress could be discerned and the following classification became useful in therapy (51).

Stage I. "Incipient crisis": Obvious respiratory difficulty may not be present.

TABLE V

*Clinical Stages as a Guide for Therapy in Myasthenia Gravis**

Stage of Crisis	Edrophonium Response	Management	
		Medication	Airway
I. Incipient	Brittle	Discontinue	Tracheotomy
II. Objective	Myasthenic	Anticholinesterase	None
	Cholinergic	Discontinue	Tracheotomy
	Brittle	Discontinue	Tracheotomy
III. Apneic	Not performed	Await airway control	Control sequence

* Reprinted from Blaugrund et al, permission granted from *Annals Otol Rhin and Laryn* 73:618, 1964.

Ventilometry may show some decrease in tidal volume and vital capacity. This type is most often seen in "brittle myasthenia" and is characterized by bulbar manifestations such as pooling of secretions, and dysphonia due to paresis of the vocal cords. Dysarthria and dysphagia are usually prominent. Although all manifestations of the crisis are not present, they are likely to supervene.

Stage II. "Objective crisis": Objective evidence of ventilatory distress is present. There is (a.) decreased vital capacity, (b.) high or rising blood pressure is present, (c.) cyanosis, (d.) decreased respirations with diminished breath sounds. Because of underlying muscular weakness, cardinal signs such as intercostal and suprasternal retraction with flaring of alae nasae are frequently absent. Because of poor ventilatory exchange, accumulation of secretions from loss of laryngopharyngeal reflexes in myasthenic or from excessive secretions in cholinergic states may not be detected.

Stage III. "Apnea": Patient has stopped breathing. Apnea may occur suddenly and unexpectedly in a patient who seemingly has been under adequate control. On the other hand, the apneic state may progress from either or both of the earlier stages.

The foregoing are primarily theoretical considerations. Each stage may follow the other with extreme rapidity or may be skipped. The patient may not be able to give a history and clinical data may not be known to the doctor on the scene.

The dictum of choice is then to reestablish a functional airway, restoring ventilation and gas exchange. Then mechanisms and solutions may be sought at leisure. Endotracheal intubation and support by Ambu Bag or by IPPB respirator, is coupled with scrupulous tracheobronchial toilette as soon as consciousness is restored in Stage III. A cuffed endotracheal tube is preferred, though with awareness of the potential of tracheonecrosis. In most patients, use of compressed air is desirable, avoiding the possibility of irritative tracheobronchitis attendant on the use of 100 percent oxygen. Cardiovascular survey is important, particularly in the older patient whose tolerance to anoxia is much shorter.

Once an airway is established, assessment of the nature of the crisis can be determined. Proper history, if obtainable, and physical examination may be most helpful. Increasing myasthenic weakness without attempted increase of anticholinesterase drugs or rapid progression of the myasthenic deficit suggest that the crisis is myasthenic in nature. Correlation of such increased weakness with intercurrent infection, emotional trauma, cessation of drug intake, or onset of menses suggest this type of crisis also. It should be noted that increased secretions may be present not reflecting muscarinic side-effect, but merely consisting of pooling and dysphagia. This sign is important because it may be mistakenly thought to be cholinergic toxicity. If one can be certain of such facts and obtain further corroboration by a markedly positive edrophonium test, cautious administration of parenteral pyridostigmine may be instituted with dramatic effect.

If the patient gives a history of increasing weakness and increasing dosage of anticholinesterase drug intake, the probability is that overdosage is the cause. Miotic pupils, bradycardia, excessive secretions, and muscarinic reactions such as gastrointestinal manifestations are present. Yet the patient may be totally flaccid, representing complete nicotinic ganglionic blockade. If cholinergic crisis is suspected, edrophonium testing should be avoided (30). With an adequate airway the dangers are lessened. Treatment is based on avoidance of further anticholinesterases, ablation of muscarinic side-effects with atropine, and general supportive measures (117). Para-amino-aldoxime has been advocated for the specific reversal of cholinergic toxicity. Our experience indicates that the theoretically stoichimetric reversal of anticholinesterase action by this drug is seldom obtainable and that serious peripheral vascular collapse may result (117). A more limited experience does indicate some value of this modality when toxicity occurs in patients who are being treated with long-lasting quaternary ammonium compounds of the phospholine iodide type (48).

A history suggesting "brittle crises" as defined above, with a varied physical picture leading to a diagnosis of this third type of crisis, is handled in the same manner as cholinergic crisis. The salient difference in management between these two types is that there is little benefit to be obtained by temporizing in performance of a tracheostomy. If cholinergic toxicity is likely, particularly Stage II, then one may defer this operation and continue with endotracheal ventilation under careful control for up to 72 hours. Kornfeld et al (118, 119) have reported from our laboratory that traces of C^{14}-pyridostigmine can be found in urine of myasthenic patients for this period of time. By that time, cholinergic toxicity should have disappeared. If not, tracheostomy must be performed. Following such emergency management it is best to admit the patient to an Intensive Care Unit for further treatment.

Because of the possible necessity for repeated tracheostomies in a myasthenic and in consideration of a possible subsequent thymectomy, this operation must be performed somewhat differently in the myasthenic patient. Attention to selection of the first or second cartilaginous interspace and use of a horizontal skin incision are important.

Management of crisis leads quite naturally into management of the thymectomy patient (120, 121). This represents one of the most significant advances developed in our institution. As late as 1961, a monograph from The Massachusetts General Hospital detailed careful neostigmine titration intraoperatively but did not give any answers as to how to deal with the apparently unavoidable postoperative cholinergic state (31). We recognized that in contradistinction to any other surgical intervention in the myasthenic, when operation was that of thymectomy, there was an invariable complete drug remission upon completion of surgery (105). While patients only rarely go into complete remission, almost all patients go into a drug remission lasting from 12 to 48 hours in duration. If medication is continued or reinstituted too early following thymectomy, the possibility and likelihood of cholinergic toxicity exists (47).

The following technique has thus been evolved. On the morning of surgery, the patient is given a parenteral dose of anticholinesterase drug, usually under-

TABLE VI

Spontaneous Remissions by Clinical Classification

Classification	No. of Patients
Group I	86
Group II A	77
Group II B	19
Group III	8
Group IV	14
Juvenile	17
Total	221 (22%)

Total Number of Multiple Remissions 37.

cutting the parenteral-oral relationship by ⅓ or ½. The purpose is to maintain respiratory adequacy only to the time of intubation. All other signs of muscle weakness are disregarded. Upon recovery from anesthesia the patient is taken to an Intensive Care Unit where appropriate monitoring can be carried out with the patient constantly being "staged" as for crisis.

When the need for anticholinesterase medication returns (as indicated particularly by decreased tidal volume and vital capacity, which is confirmed by careful edrophonium testing), anticholinesterases are again given with following safeguards: 1. intravenous administration so that there is no question of absorption of dose; 2. dosage is by one-half to two-thirds undercut as compared to usual requirements and is titrated particularly for respiratory performance; 3. there is recognition that the dose schedule must be on a demand basis as there is usually a prolonged effect of 2 to 3 times the usual preoperative "dose period" for the first few doses.

Since this requirement for anticholinesterase drugs in the postoperative period has little or no bearing on the eventual dose or to the eventual surgical result; and since the patient's response is most variable, we do not aim for total optimal strength. One is satisfied with respiratory adequacy and preferably improvement of cough reflex and dysphagia. If achievement of these aims is coupled with development of muscarinic side-effects, particularly that of troublesome increased secretions, administration of anticholinesterases may again be totally stopped until edrophonium testing guides its reapplication. If copious secretions become a problem, the patient is supported with the use of IPPB respirators and tracheal toilette through the tracheostomy. Availability of compact, easily applied IPPB devices of lesser or greater sophistication has been of inestimable help. While the Bird type of respirator had been our mainstay, particularly in the era of sternal-splitting surgery, a respiratory dependence problem had been noted and was most difficult to deal with. The patient's apprehension, incisional pain and the mechanical aid of the respirator made weaning most difficult. Until a multidisciplinary physiologic approach to the changed dead space of the tracheotomized patient was employed, and until application of constant blood gas monitoring (Astrop), these were problems relating to hypocapnea and the altered respiratory center drive. Recognition and monitoring have led to interposition of extracorporeal dead space and to application of different types of support devices.

By the fourth to fifth postoperative day, there is returning function of the gastrointestinal tract and stable predictable anticholinesterase requirement. Resumption of oral therapy may then begin, perhaps at first with the liquid form of pyridostigmine which is easier to swallow or may be easily passed via a nasogastric tube. While again, the aim is not that of optimal strength in all areas, the limits of muscle power are tested more fully. It is not desirable to change dosage or periodicity more often than every 24 to 48 hours (30).

For several years we advocated the use of broad spectrum prophylactic antibiotics in the postthymectomy management of the myasthenic patient. Recent experience suggests that it is better to apply the same demand basis to this form of therapy with careful control by appropriate cultures. When a patient comes to surgery with a preexisting and at times unavoidable tracheostomy, antibiotics may be required immediately.

In the occasional patient, immediate postoperative remission is extremely brief and clinical course is again stormy from a myasthenic point of view. While this in no way prognosticates ultimate outcome, thymectomy in such patients appears not to have helped at all and has added the burden of surgery. In such patients, early postoperative administration of a course of ACTH may be extremely helpful. This is analagous to the preoperative use of ACTH to achieve a state compatible with safe surgery.

Outpatient Care

Fortunately only a small portion of the myasthenic patient's life is spent either in clinic visits, in the hospital, or in the office of specialized physicians. Incidence of myasthenia gravis creates a "center" concept to cover a wide geographic area and patient group who for most of a given year will be under the care of their private local doctors.

Specialists in myasthenia gravis are often called upon for advice to help in the care of the patient during intercurrent disease, to regulate fluctuations of the myasthenic deficit, and to determine how this disease affects their total health picture. Experience in such an advisory capacity permits a distillation of the most commonly encountered problems. As is common in other chronic disease states, the severe hospital cases discussed in previous sections (representing, fortunately, only a small percentage), often give a skewed picture as to the severity of the disease in the total myasthenic population. The overwhelming majority of myasthenics lead useful productive lives with only minor deficits. Myasthenic drug requirements constitute a major share of the questions asked. Because of the spontaneous variability of the disease and the effect of a host of external influences, it is important that both the patient and his physician understand that the most certain feature of myasthenia is its changeability. Such change may be expected in a 24-hour period relating to activity and is certain over a period of months; it must be met with a flexibility of concept and drug management. Priorities of deficit importance must be reevaluated constantly as there may be a dichotomy of drug action such as improvement in ptosis with worsening of diplopia.

The patient learns recognition of toxic states. He will accept alteration of drug action and will learn not to "juggle" dosage and thereby court cholinergic toxicity. There are also fixed deficits resulting from "burnt-out disease" in muscle groups which no amount of medication will repair, yet in whom cholinergic ganglion blockade may still occur, if there has not been complete remission. Inherent in the education of the patient is emphasis of the potentials of the disease leading to drug automatism and to overdosage. Any chronic disease with this impact seriously alters the fabric of life, particularly in the second and third decades, with resulting emotional and social maladjustments. A young woman, for example may totally have to rearrange her life and personal horizons. However, most of our young females get married and have children.

When diagnosis is first made, depending on disease tempo and classification, evaluation must be frequent, perhaps beginning with close observation in hospital for initial therapy. Such hospital stay is recognized to be an artificial setting, secure for the patient, rich in tutorial possibilities, but quite different from day to day life. The patient becomes familiar with the anticholinesterases, learns his or her own response, absorptive capacity, daily rhythm and begins to understand development of toxicity by having careful explanations of muscarinic side-effects. The timing of doses with relation to getting up, ingesting food and the potential need for administering drugs at night, are all evaluated and explained. Dysphagia, for example, is best handled by timing drug administration to occur ¾ to 1½ hours prior to meals. Severe dysphagia at time of first morning dose may be handled by a preliminary intramuscular edrophonium injection, which will permit pill or syrup deglutition if nocturnal Timespan® adjustment fails. This emergency administration of edrophonium is most useful when sudden unexpected disease acceleration supervenes.

When the patient is discharged he is encouraged to keep an hourly log over the course of 1 to 2 weeks, indicating reaction over a day as related to drug ingestion and side-reactions. Perusal of such a log over a week's time permits the physician an insight into the high and low spots of drug response leading to customized dose and time variation. Even with such sophisticated adjustments, there will still be good and bad days and one encourages a degree of forebearance rather than rapid dose and time changes. When one considers the additive effects of rest to any anticholinesterase regimen, it becomes clear that it may well be wise for a severe myasthenic to have the major meal of the day in the morning when mastication and deglutition are at their best. Indeed such periods of rest, which is a major part of the therapeutic regimen, should be invoked when prolonged and potentially tiring periods of activity are contemplated. These rest periods need not be of long duration. Frequent five-minute rest periods are preferable to a more prolonged one.

Through initial edrophonium testing, both patient and doctor learn what can be expected in terms of repair of disease-induced defects and then can set realistic goals. This type of testing permits definition of which commonly used anticholinesterases may be best for a given patient. Selection of adjuvant drugs should follow a longer baseline study.

If muscarinic side-effects supervene at therapeutic drug levels, the patient is taught the use of atropine and Lomotile®.

The patient's course will determine subsequent therapy. The clinical classification is a dynamic concept with an initial and a current evaluation. Either upon initial presentation or soon thereafter, depending upon clinical classification, an overall prognosis and treatment plan are often determined. The present concept is that patients with the characteristics of Group III should be considered candidates for very early thymectomy. This group does not permit long observation as do the milder forms of the disease, where its characteristics and inexplicable spontaneous remissions may play a prominent role.

Perhaps, the most happy prognosis other than in the neonatal form of disease, occurs in Group I, the ocular form. Here persistence in this locus, with no spread for two years, almost assures no further advance of the disease. However, such ocular symptoms may become fixed and irreversible (burnt-out disease). One does not consider this type of patient for thymectomy. While other milder forms of the disease, where there is poor control, may be considered for thymectomy, present knowledge puts one on guard against the patient's desire for this procedure. Lower morbidity by the transcervical technique may lead to further broadening of our current indications for thymectomy, possibly without obligatory tracheostomy in selected cases. Advice concerning other modalities of therapy such as ACTH will depend upon the patient's course.

Like other individuals, myasthenic patients sustain fractures, develop colds, become pregnant, undergo laparotomies, are subject to dental caries, and also unfortunately develop heart attacks. They may have severe disagreements with employers, children, and spouses. In all of these instances, adjustment and reaction must often be couched in terms of their myasthenic state. Awareness of anesthetic, antibiotic, and other drug reactions on myasthenics must be inculcated. Our dictum is conservatism and avoidance of any complications whenever possible. We are thus more prone to administer influenza vaccine, prescribe antibiotics for minor infections, and in all ways protect the patient during any intercurrent event. Suggested is strict control of weight gain in pregnant and nonpregnant myasthenics and insistance upon close obstetric supervision. It is recommended that no surgical procedure be carried out in a setting not equipped for myasthenic emergencies. Careful, constant appraisal of the patient's psychoemotional status is suggested.

The prognosis in myasthenia gravis has greatly improved in the past two decades. There still are, unfortunately, a percentage of fatalities directly attributable to this syndrome. This group of patients is primarily limited to Clinical Group IIB, III, and IV. It is interesting to speculate on the number of deaths related to cancer in patients who, because of our clinical advances, have been granted greater longevity; and whether such deaths should be considered myasthenic (10). This is more fully discussed in a following report in this issue.

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Studies in Myasthenia Gravis: Biologic Aspects

ALLYN H. RULE, PH.D. AND PETER KORNFELD, M.D.

Introduction

Physiologic, neurologic, pharmacologic, endocrine, immunologic, and viral mechanisms have been postulated as active factors in myasthenia gravis. Yet, almost 300 years after its initial description, little is known about the onset or etiology of this so-called "autoimmune" disease. Different eras have favored various approaches to the study of myasthenia gravis in the laboratory, depending upon the theory in vogue and upon the limitations of the various clinical and laboratory methodologies available at the time.

Present interest in cellular immunology, viral oncology, viral-induced anergy, and the role of the thymus (or thymus-derived lymphocytes) in the recognition of "self" and foreign antigens has stimulated new avenues of investigation in myasthenia gravis. The role of thymectomy in experimental animal model systems including transplantation rejection, immune response, autoimmune phenomena, carcinogenesis, and potential viral interactions has increased interest in a disease in which thymectomy has become standard therapy.

Patients with myasthenia gravis form a unique human population with thymic abnormalities. These often include thymomas and persistent thymus, each with or without the presence of germinal center hyperplasia (1, 2). Clinical coexistence of myasthenia gravis either with cancer or another so-called autoimmune disease far exceeds anticipated probability (3, 4).

Thymectomy, frequently performed in this disease, gives increased assurance of remission. However, clinical benefits are often delayed for several years. Significant clinical improvement is also noted with use of ACTH, possibly with corticosteroids, and perhaps with immunosuppressive therapy (5). Preliminary data suggest that thymectomy may also lessen the increased incidence of cancer in this population (3).

The presence of lymphorrhages (6), lymphocytes sensitized to muscle components (7), and circulating antibodies both to muscle and thymus (8) in patients with myasthenia gravis provoke the thought that autoimmune processes may be involved at certain stages in this disease. As yet, however, disease initiation seems more related to some unknown factor.

Electron micrographs of the dedifferentiated, embryologic forms of muscle endplates present in many myasthenics suggest changes at the DNA-RNA level of interaction, as well as degenerative alterations (9). Decreased availability of acetylcholine and the action or lack of action of unknown "trophic" factors may also provoke neuromuscular deficit (10). The presence of antibodies, cells sensitized both to nerve and muscle and their interaction with each other as well as with surrounding tissue may well invoke locally the soluble (11) and chemi-

From the Department of Medicine and The Myasthenia Gravis Research Laboratory of Mount Sinai School of Medicine of The City University of New York, N. Y. 10029.

cal substances (12) of delayed hypersensitivity. Presence of these factors would cause membrane damage, changes in permeability, phagocytosis, renewed immunologic injury, and further responses. Certainly, however, in many myasthenic patients immunologic abnormalities may be few or nonexistent, and no evidence of viral infection exists. Yet, thymectomy yields its best prognosis in this group (1). Thus, studies of symptoms, etiology, and potential methods for investigating this disease have been and remain fragmented.

The need for a review of past, present, and current clinical and experimental research approaches to myasthenia gravis seems appropriate. The purpose of this study was to evaluate the laboratory and interrelated clinical data accumulated at many research centers. The historical relationship of these studies to newer hypotheses and research approaches is presented.

Historical Background

ERA OF DESCRIPTIVE CLINICAL PHYSIOLOGY, 1658–1905

The earliest era of systematic inquiry into the disease processes of myasthenia gravis concerned itself with descriptive anatomy and physiology.

Peripheral limb weakness and diplopia were first described in 1658 by Mallet (13) and expanded by Willis in 1672 (14). Dysarthria, dysphagia, diplopia, and respiratory failure were noted. Of importance was the report by Wilks (1877) and confirmed by Oppenheim in 1887 that autopsy revealed no apparent disease of the central nervous system in myasthenia gravis (13).

Differences between the neurologic symptoms of true bulbar palsy and myasthenia were pointed out by Goldflam in 1893. The general absence of muscle atrophy and fibrillation in the presence of muscle exhaustion with repetitive stimuli was noted (13). In 1895 Jolly made the important observation that exhaustion in one group of muscles induced weakness in other nonstimulated groups, suggesting the presence of a circulating neuromuscular inhibiting factor. Rediscovered by Dr. Mary Walker in 1934, this phenomenon now bears her name. Jolly was also responsible for naming the disease "Myasthenia Gravis Pseudoparalytica" (grave muscle weakness), the name accepted by the Berlin Society of Psychiatry and Neurology in November 1899.

The first report of a thymic tumor was noted in 1901 (15). As early as 1905, Buzzard suggested morphologic changes at the myasthenic neuromuscular junction (15). After 1900, numerous reports described clinical characteristics of the disease. Indeed, this early descriptive era of investigation concluded with the now widely accepted clinical classification (see clinical section).

ERA OF NEUROPHYSIOLOGY, PATHOLOGY, AND PHARMACOLOGY, 1932–PRESENT

Discovery of the chemical mediation of neuromuscular transmission via acetylcholine in 1932–3 by Loewi opened an era of neurologic pharmacology in myasthenia gravis (16). In 1936 Sir Henry Dale reported that acetylcholine liberated at motor-nerve endings in striated muscle was limited by the action of acetylcholinesterase found in the synaptic cleft (17). Electromyographic investigations began to examine the nature of the muscle twitch in normal and myasthenic muscles. Pharmacologists, meanwhile, tried to isolate the circulating substance responsible for the Walker effect without success (13).

The earlier discovery in 1934 that physostigmine exerts beneficial effects on muscle weakness in myasthenia was an important step toward and the beginning of modern concepts of therapy in this disease. Shortly after this, Aeschilman's analogue of physostigmine, neostigmine, was utilized. Subsequently other analogues became available, and clinical trials of several beneficial drugs by our own group at Mount Sinai have since appeared (see clinical section).

Recent studies with C^{14}-pyridostigmine in our laboratory suggest that myasthenic and normal individuals show similar metabolism of this most widely used anticholinesterase drug (18). Neither the drug nor its metabolites are protein-bound in the bloodstream. After a single intravenous dose, 90% of the radioactivity can be recovered in urine, and traces of C^{14}-pyridostigmine are still detectable in urine 72 hours later. While pyridostigmine is chiefly metabolized in the liver, multiple metabolites have been demonstrated in urine.

Plasma C^{14}-pyridostigmine disappearance studies indicate that a threshold blood level exists. Distribution studies suggest that once pyridostigmine leaves the bloodstream, it no longer available for recirculation and subsequent action at the motor endplates (19).

Use of drugs which decrease acetylcholine breakdown at the synaptic cleft eventually led to the idea that the quantal release or usage of acetylcholine was affected in myasthenia gravis. Studies in the 1950's through 1970 revealed two sites of such action. Their resultant effects on muscle-nerve interaction were also indicated.

1. Presynaptic phenomena in myasthenia gravis. These phenomena might include the "active" transport of choline back into the nerve, the synthesis of acetylcholine, the amounts of acetylcholine contained in presynaptic vesicles, the mobilization of acetylcholine packets, and the release and/or changes in local calcium concentrations which lessen or increase the number of acetylcholine quanta released by each nerve impulse (10, 20–23).

Trophic neurogenic factors and axon injuries have been shown to affect acetylcholine release and neuromuscular transmission (24, 25). Regardless of the mechanism involved, the quanta of acetylcholine released must allow depolarization of the muscle endplate. A 15 to 20 mV threshold is thus involved. The concept of lessened acetylcholine available for utilization is the basic thesis of those favoring a presynaptic neurologic phenomenon.

Concomitant studies of normal human intercostal muscle indicated that 4.04×10^{10} molecules of acetylcholine are stored in an individual motor endplate releasing 218 quanta of acetylcholine (26). While 650 quanta of acetylcholine can be hydrolyzed per minute, the acetylcholine released is only a fraction of the total acetylcholine stored at the synapse. Katz et al showed that miniature endplate potentials are capable of releasing 100 to 200 packets of acetylcholine (27). Each packet contains several thousand acetylcholine ions (26). Thus, each miniature endplate potential is the result of one quantum of acetylcholine delivered to the postjunctional membrane. In man, acetylcholine is synthesized from choline in the presence of tetraethyl pyrophosphate. Intracellular diphosphoesterase interferes with this synthesis. It has been shown that xanthines interfere with these esterases and allow the accumulation of cyclic adenosine monophosphate (CAMP) (28). One of the forces responsible for decreasing the force of muscle contraction is inactivation of myofibrils in the core of the muscle fiber. Caffeine (xanthine) antagonizes this inactivation by diphosphoesterase, changing the length-force relationship of short muscle lengths (29). Rüdel and Taylor believe that this effect is due to the more effective membrane depolarization in the presence of caffeine.

Thesleff has shown that muscle endplate potential of myasthenic intercostal muscle is only 20% that of normal muscle (30). He concluded that resultant muscle weakness in myasthenia gravis is caused by significant reduction in the size of acetylcholine quanta, though not necessarily a numerical reduction. Desmedt also concluded that the basic defect was due to the impaired synthesis of acetylcholine on the basis of defects in neuromuscular transmission observed in hemicholinium-treated muscles (10).

Takamori and Gutman recently reported a myasthenic patient in whom electrophysiologic data suggested an intermittent defect of acetylcholine release superimposed upon the more classic defect, the reduction in quantum size (31). Thus, presynaptic blockade can depend on nerve action potential amplitude, on extracellular ion concentrations such as calcium; on active transport of precursor metabolites; on enzyme syntheses; and on release of unknown factors governing acetylcholine release (10). Other investigators favor a second site to explain the increased weakness in myasthenia gravis.

2. Postsynaptic phenomenon in myasthenia gravis. Depolarization by acetylcholine depends upon postsynaptic chemical receptors with which acetylcholine forms temporary links. This linkage causes local changes in ion permeability, depolarization, and the propagation of an excitation potential which triggers the contractile mechanism of muscle in an all-or-none fashion. Receptor molecules may be reduced by the presence of a blocking agent such as d-tubocurarine or by previous exposure of the muscle endplate by depolarizing substances which render the membrane insensitive to the action of acetylcholine (32).

Normally muscle membrane depolarization spreads inward via transverse tubules resulting in calcium ion release from sarcoplasmic reticulum which is related to the Z line microscopically. These calcium ions interact with myofibrillar proteins and adenosine triphosphate, allowing formation of bridges between myosin and actin. Contraction follows.

Initial suspicion of increased acetylcholinesterase activity at the neuromuscular junction in myasthenics has not been borne out by histochemical studies. Bickerstaff et al found no significant differences in acetylcholinesterase distribution in normal as opposed to untreated myasthenic endplates (33). Under in vivo conditions, acetylcholine-activated postjunction membranes become permeable to Na^+ and K^+ ions. This effect lasts only a few milliseconds.

Endplate potentials last slightly longer because the postjunctional membrane must be passively recharged. Acetylcholine-induced activity is brief because of the rapid hydrolysis of acetylcholine and its rapid diffusion from the synapse. Namba and Grob have shown that the turnover number of acetylcholine per active cholinesterase site varied from 2.07 to 18.3 × 10^5 molecules, while the turnover time per acetylcholine molecule is 33 to 289 μ seconds (34).

Decreased sensitivity of the myasthenic endplate to acetylcholine has been observed by many investigators to result in choline-insensitive block versus acetylcholine-reversible or competitive block. Patients with acetylcholine-insensitive or depolarizing block respond poorly or not at all to anticholinesterase medications. They will probably develop increasing weakness and fasciculations if medication is continued. It is not clear whether the decreased sensitivity of myasthenic endplate to depolarizing effects of acetylcholine is due to an alteration in receptor proteins which may be synonymous with membrane-bound acetylcholinesterase or due to prolonged exposure of a depolarizing substance.

Parisi et al have demonstrated that a special proteolipid which is present in Electroplax membrane is able to bind cholinergic agents and may represent a cholinergic receptor (35). Electromyographic studies on single myasthenic muscle fibers have revealed that different motor endplates within a single muscle fiber are affected to a different degree, some being entirely normal (36). All instances of myasthenic endplate block can thus not be adequately explained by present pre- or postsynaptic physiologic mechanisms. However, although the postsynaptic concept held major interest through the 1950's, the presynaptic mechanism gained ascendency at the Third International Conference of Myasthenia Gravis in 1965. At the most recent conference in 1970 evidence was presented to support both mechanisms.

Morphologic changes both of normal axons and endplate structures have been found early in myasthenia gravis by several investigators (37, 38). Terminal endplates were elongated and multiple endplates were observed upon single muscle fibers. Enlarged areas of histochemical cholinesterase activity were apparent. These data suggested that formation of new secondary synapses around the original endplate had taken place. Macdermot, however, pointed out reports of endplates in myasthenics who had been resistant to neostigmine therapy and he interpreted this to imply primary neural changes (37). Clinical significance of these anatomic variations was less clear. Why did many of these patients respond to anticholinesterase drugs in the presence of these structural changes? It was impossible to say whether these structural changes were primary or represented a secondary, compensatory mechanism.

Axelsson, Thesleff, and Miledi had shown as early as 1959 that the motor axon had a trophic effect on neuromuscular transmission (24, 25). They showed that interruption of a motor axon greatly extended the proximal area of maximum acetylcholine sensitivity away from the original synaptic area. It was postulated that such axon injury might lead to a change in the extrajunctional muscle surface membrane and might secondarily stimulate elongation, tortuosity, and realignment of the endplate, e.g., compensatory effect. Subsequent electronmicroscopic work by Bickerstaff suggested poor development of junctional folds but apparently good preservation of synaptic vesicles (39). Wolf reported that the number of such observed vesicles was definitely reduced in degenerating endplates (9). He also reported that in neostigmine-fast fatal cases of myasthenia gravis, the endplates were unable to elongate and arborize. He postulated that the Schwann cells eventually "usurp" the synaptic position of the shrinking terminal axon expansion.

Other investigators have reported the widening of the synaptic clefts within the endplate, suggesting degeneration primarily in the postsynaptic apparatus. More recently, Engel and Santa have presented their electronmicrographic data in myasthenic patients (40). The mean nerve terminal area and postsynaptic membrane length were definitely decreased while synaptic vesicle diameter and content per nerve terminal area were normal. Newly formed growing nerve terminal end bulbs, immature and dedifferentiated endplates, denuded of their nerve terminals, were also frequently seen. Bergman et al reported the finding of elaborate subneural apparatus on mounds of relatively undifferentiated sarcoplasm in myasthenic endplates (41). Nerve endings were sparse and Schwann cells, myelin sheaths, and axons showed degenerative changes. Capillary endothelium also seemed damaged and the basement membrane appeared thickened in many sections obtained from myasthenic muscle.

In a study of 30 patients the presence of denervation atrophy (63%), fiber atrophy (50%), chronic necrosis (30%), lymphorrhages associated with muscle fibers (23%), acute fiber necrosis with phagocytosis (7%), and the presence of "inclusion bodies" (10%), and histopathology "not unlike that of certain viral or viral-suspect diseases" (10%) were found (6). Recent studies of the similarities between embryologic and myasthenic endplates suggest dedifferentiation at the DNA-RNA level. These data suggested that the plethora of unique physiologic and morphologic changes found in muscle-neuron interactions present in myasthenia gravis might be due to random effects of viral "infection" or viral interaction at the host genome level in either muscle or nerve elements rather than any visibly consistent mechanism of neurologic origin. Viral induction of these morphologic changes requires confirmation.

Some, but not all, of the changes in the neuromuscular junction have been related to the presence of lymphorrhages secondary to inflammatory changes (9). Such studies suggest the need for newer investigations relating changes in motor endplates to local effects of cellular hypersensitivity.

THE AUTOIMMUNE ERA, 1956–PRESENT

Humoral Antibodies, Serum Complement

An autoimmune approach to myasthenia gravis began with the observations of Nastuk, Osserman, and Plescia in 1956 that serum complement levels correlated inversely with the severity of the disease (42). This initial observation was regarded as indirect evidence that immunologic reactions were involved in myasthenia gravis.

In 1959 Nastuk, Strauss, and Osserman showed that myasthenic sera were able to lyse surface cells of frog sartorius muscle (43). This cytolytic activity paralleled the sera's ability to reduce twitch tension in an indirectly stimulated frog sciatic nerve-sartorius muscle preparation. This property was lost when sera were heated to 56° C for one hour. Determination of serum complement levels revealed a clinical correlation with complement levels in 46 out of 68 patients tested in 1960 (44). Complement levels fell with exacerbation of clinical disease and rose parallel with clinical improvement and remission. This was strongly reminiscent of complement activity in sera from patients with systemic lupus erythematosus. Decrease in complement levels suggests fixation in an immunologic reaction between antibodies and one or more components of muscle and/or nerve.

In 1960 Simpson noted high incidence of autoimmune disorders among 440 myasthenic patients and postulated a possible autoimmune mechanism for the neuromuscular bloc strictly on hypothetical grounds (45).

The presence of circulating antibodies in sera obtained from patients with myasthenia gravis which reacted specifically with striated muscle was first described by Strauss, Seigal, Hsu, Burckholder, Nastuk, and Osserman that same year (46). Presence of antibodies to skeletal muscle in myasthenia gravis has now been confirmed by many laboratories. Investigators include Beutner et al (47), van der Geld and Oosterhuis (48), Feltkamp et al (49), Grob and Namba (50), Thivolet and Kratchko (51), Djanian et al (52), and Adner et al (53). Many laboratories interpreted the presence of antibodies to muscle as suggesting autoimmune involvement.

Circulating antibodies to striated muscle have been found by complement fixation (42, 46, 54), precipitation in Ouchterlony gel (54–56), passive hemagglutination (52), and by direct and indirect immunofluorescence using striated muscle as substrate (4, 46, 52, 54, 57). In addition, immunofluorescent assays using "myoid" cells of thymus (58, 59) or cardiac muscle (52) have also been shown to react positively with myasthenic sera. All other tissue substrates, including smooth muscle, do not react. Overlap between serum positivity as measured by immunofluorescence, passive hemagglutination, and/or precipitation in Ouchterlony gel as measured either by their reactivities or titers have been observed in many laboratories. In our laboratory the combination of all three methods yields positive reactions in 54% of sera obtained from patients with myasthenia gravis (60), whereas the indirect immunofluorescent test for muscle antibodies by itself was positive with 30 to 40% of our sera (61). This figure was in agreement with those obtained by Beutner's laboratory (57).

The use of the polarizing microscope and the ultraviolet fluorescent microscope and immunohistologic techniques have aided in localizing the general site of the antibody-antigen reaction in muscle fibers. In general, morphologic appearances have indicated that lateral portions of A-bands contain the most active antigenic component (46, 62). The A-band, or anisotropic band, of muscle usually contains both actin and myosin which are normally combined in the form of an actomyosin-ATP complex. The I-band, or isotropic band, contains actin. Staining of the A-band might suggest that actomyosin or myosin would contain the active antigenic determinant. Many laboratories utilizing muscle from such diverse sources as man, rhesus monkey, rat, guinea pig, mouse, rabbit, ox, dog, and frogs have confirmed these studies (46, 52, 56). Vetters' descriptions in 1965 (63) and 1967 (64) of I-band staining with sera obtained from patients with myasthenia gravis has been confirmed by Strauss and Kemp (65). Additional studies by Vetters showed that both A- and I-band staining occur (66). The degree of muscle contraction present at time of fixation imposes artifacts which can be partially resolved with the use of a polarizing microscope. Resolution is impossible with this method at the molecular level.

Search for autoantibodies directed at the neuromuscular endplate has been unproductive so far. In one study by Namba and Grob, sera obtained from patients with myasthenia gravis were absorbed with dried muscle powder to remove muscle antibodies. After this exhaustive procedure, weak staining of endplates was found in only 2/3000 preparations (67). Nonspecific uptake of gamma globulin by muscle leaves negative conclusions concerning the presence or absence of antibodies to the endplate open to reexamination with more sensitive methods which are independent of the absorption of antibodies by muscle for demonstration of specificity. The antibody consumption test with muscle is based on the differential uptake of immune myasthenic versus nonimmune normal sera by muscle preparations (68).

Electronmicroscopy with its high power of resolution has also failed to indicate absolute localization of antigenic sites located in muscle substrates. Although the A-band proteins consistently interacted with ferritin-labeled antibody, the reaction was shown to be nonspecific. Both normal and myasthenic sera reacted in similar fashion (69, 70).

Investigations were begun in this laboratory in 1970 to isolate, purify, and immunochemically characterize human muscle fractions (54). Analysis of reactions obtained by microcomplement fixation revealed that actin was an inactive antigen. While actomyosin yielded reproducible, stable reactions from lot to lot of muscle, the most highly reactive, yet least stable, antigen was myosin. Heat stability studies showed that freezing and thawing only slightly altered actomyosin reactivity. Twenty to 30 percent of the activity remained when heating actomyosin at temperatures of 37°, 47°, and 57° for 40 minutes at protein concentrations of 4 mg/ml. Conversely, while myosin lost much activity with freezing and thawing, little was lost at 37°. All activity was lost at 47°, 57°, and 80°C with similar preparations. Myosin lost 50% of its activity at 4°C within two weeks, whereas actomyosin lost little or no activity. All fractions had to be processed quickly within a week at 4°C for maximal yields and activity.

Structural analyses of myosin show that it contains two heavy chains and up to five light chains—the latter possessing the physiologic activities of this molecule (71). Between 30–40°C the myosin molecule loses its light chains (72). Antigenicity was also lost at temperatures above 37°C. A final ammonium sulfate purification step which allows analysis of myosin in the optical ultracentrifuge also resulted in loss of antigenicity. This too, may have been due to loss of the light chains.

The light chains contain ATPase, ATP-binding and Ca^{++}-binding sites in muscle. These data are in agreement with the discovery by Namba and Grob that muscle fractions rich in ribonucleoprotein were highly antigenic (67). The fact that immunologic activities of their preparations could be inhibited by ATP, ribonuclease, d-tubocurarine, or with chymotrypsin are not at variance with our concept that the light chains of myosin contained the antigenically active site. Myosin contains 1½ binding sites for ATP while actomyosin contains ½ site. Thus, the light chains are also active in binding actin to myosin. Protection of these biochemically active sites in actomyosin at 37°, 47°, and 57° suggested that binding of actin to myosin affords both immunologic and physiologic protection for these light chains in vitro although bonding of light chains to actin lowers antigenicity.

Circulating antibodies may possibly be directed at the ATPase, ATP, Ca^{++}-binding, and other sites of muscles and endplates. It is conceivable that simultaneous presence of sensitized lymphocytes and antibodies to muscle cell elements act concurrently to produce immune damage which may lead to defective neuromuscular transmission. It seems unlikely that antibodies alone play an active part in the disease process by merely circulating in the bloodstream. Indeed, the number of unsuccessful animal models for myasthenia gravis using this approach reinforce this interpretation. The injection of thymus, purified thymin, and muscle in complete Freund's adjuvant has been shown to produce transient changes in electromyographic patterns resembling myasthenia gravis. Antithymus and antimuscle antibodies have also been produced in these animals. However, these animals do not have the clinical disease (73).

In our laboratory we have begun to correlate relationship of humoral antibodies to cellular hypersensitivity. Many patients with myasthenia gravis manifest in vitro delayed hypersensitivity to crude muscle (7). Although some patients exhibited cellular hypersensitivity without significant antibody titers, no myasthenic patients had antibody titers of significance without migration indices of significance. These data suggest that presence of lymphocytes sensitized to muscle in addition to circulating antibodies may be important factors in certain stages of the pathogenesis of myasthenia gravis (Fig. 1).

It is known that antibodies are not normally produced to the "active site" of enzymes nor to highly evolved and specialized molecules (74). Antibodies do have the ability to alter activity of such molecules in a less striking manner by forming antibodies to adjacent sites. Binding of antibodies to nonactive sites may cause steric rearrangement of the molecule. These alterations may prove to cause partial, or up to 95%, inactivation of the molecules' normal activity.

Antibodies to either ATPase, ATP-binding or Ca^{++}-binding chains of myosin might produce multiple physiologic alterations in energy sources for muscle contractions and in transport of important metabolites through membranes. Changes in calcium-binding potential might affect muscle membranes and the effectiveness of acetylcholine in causing local depolarization and excitation at the endplate.

Any or all of these mechanisms which involve lessened activities or partial inactivations might explain the gradual decreases seen in electromyograms of the myasthenic and help to explain progressive weakness after repetitive activities. The disease pathogenesis in certain patients appears to have autoimmune

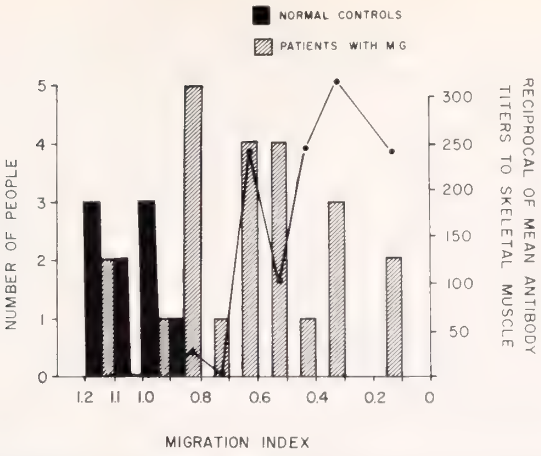

FIG. 1. Relationship between migration index and the reciprocal of antibody titers to skeletal muscle.

implications once the disease process is initiated. However, it is also possibly true that in certain patients autoimmune phenomena cannot be discerned.

A common finding in autoimmune disease is the presence of antinuclear antibodies. These were first described in 1957 by Friou (75) and identified as gammaglobulins in 1959 (76). While almost 100 percent of all patients with systemic lupus erythematosus have antibodies which will localize in the nucleus, its incidence in other autoimmune diseases varies. Reports in the literature have indicated that presence of antinuclear antibodies in serum obtained from patients with myasthenia gravis varies anywhere from 0 to 89% (4, 77–82). In our laboratory we have examined sera for the presence of antinuclear antibodies (ANA) in several "autoimmune" disease processes. These diseases were categorized according to the number of so-called autoimmune symptoms present in the same individual. No antinuclear antibodies were found in the sera obtained from 13 normal controls or sera obtained randomly from 25 noncollagen/vascular disease. The percentages of positive sera and the mean titers of antinuclear antibodies in 260 patients having one autoimmune disease varied in the following manner:

TABLE I

Antinuclear Antibodies in Patients with Various Autoimmune Diseases

	Antinuclear Factor	
	Percentage Positive	Reciprocal of Antibody Titer (Mean)
1. Scleroderma	20	10
2. Myasthenia Gravis	21	40
3. Pemphigus	29	15
4. Rheumatoid Arthritis	29	60
5. Systemic Lupus Erythematosus	100	590

The percentages of positive sera and the reciprocal of the antinuclear antibody titer changed significantly in the group in which two "autoimmune diseases" were present in the same individual. Data in 25 patients were as follows:

TABLE II

Antinuclear Antibodies in Patients with Two Autoimmune Diseases

	Antinuclear Factor	
	Percentage Positive	Reciprocal of Antibody Titer (Mean)
1. Myasthenia Gravis and Collagen/Vascular Diseases	100	55
2. Myasthenia Gravis and Pemphigus	100	105
3. Myasthenia Gravis and Rheumatoid Arthritis	90	212
4. Myasthenia Gravis and Systemic Lupus Erythematosus	100	462

Specific antibodies for one or more target systems with multiple clinical equivalents most probably represent secondary "autoimmune" complications rather than basic causative factors. Antinuclear antibodies have been found in many autoimmune diseases to varying degrees. Feltkamp, using undiluted serum found the following percentages of antinuclear antibodies occurring in his autoimmune groups: Rheumatoid arthritis, 28%; myasthenia gravis, 24%; pernicious anemia, 9%; autoimmune thyroiditis, 9%; and normal controls, 4%. All of these groups had higher incidences of antibodies to the target tissue as well as antibodies to at least four other "autoimmune" target organ systems (4).

The presence of antinuclear antibodies may be a largely nonspecific autoimmune phenomenon which represents the production of antibodies to other stimuli such as viral antigens, having cross-reactivity with the person's own DNA, nuclear proteins, and nuclear enzymes. The higher incidence of antinuclear factor with two concomitant autoimmune diseases would merely be a reflection of a more severely malfunctioning autoimmune system or, conversely, a greater degree of infectivity of the causative agent.

Lack of recognition of self may be either the direct effect of virus activity or indirect effect of changes brought about in the genetic material present in cells of the lymphoid system. The more severe and the longer the malfunction of cells of the lymphoid system, the more probable is the presence of antibodies to a target tissue or to antinuclear antibodies cross-reacting with remnants of an infective agent. In this sense, antibodies to nuclear materials rather than to the target tissue per se may be the best index of immune system malfunction.

The presence of antibodies to target tissues or to nuclear materials as yet represents a result rather than an initiating factor in autoimmune disease.

Cellular Immunity

Studies of cellular immune responses of myasthenic patients fifteen years postthymectomy were begun by Kornfeld, Siegal, Weiner, and Osserman in

1965 (83). Delayed hypersensitivity reactions were obtained to tuberculin and fungal antigens. Patients could be sensitized to 0.25% dinitrochlorobenzene (DNCB) without difficulty. Absolute lymphocyte counts were normal and none of these patients developed recurrent infections or neoplastic disease during the period of observation.

We have observed that thymectomized myasthenics are able to yield normal primary responses to triple typhoid antigen. However, only weak secondary responses could be obtained (83). Grumet obtained similar results with thymectomized mice (84). At the end of six months, 80% of the thymectomized group no longer had discernible typhoid-H titers while 67% of nonthymectomized myasthenics and the healthy control group did. No correlation was found between thymic pathology and the ability of a myasthenic patient to produce circulating antibodies or give delayed skin-hypersensitivity responses (83).

Additional immunologic studies of thymectomized and nonthymectomized patients with myasthenia gravis followed in 1966 (53). Adner et al found no abnormal humoral antibody production to plague vaccine in his myasthenic patients, but followed them for only 90 days. Their inability to sensitize 50% of the myasthenic patients to DNCB regardless of thymectomy was probably related to low concentrations of DNCB used. No immunologic abnormalities were found that could be attributed to effect of thymectomy per se (83, 53). Neither of these investigations followed the patients for a sufficiently long period of time to permit final conclusions regarding immune response in thymectomized humans. In a study by Joshua et al, direct skin testing with crude human muscle antigens yielded delayed hypersensitivity reactions in 2/17 patients with myasthenia gravis as compared to the presence of circulating antibodies in 11/17 patients (85).

These studies show that secondary responses in delayed hypersensitivity reactions and reduced circulating antibody titers may be found in thymectomized patients with myasthenia gravis or those with thymomas. While the majority of myasthenics display reactions similar to age-matched healthy controls, a low percentage will display skin hypersensitivity to muscle extracts.

Studies in cell-mediated immunity have increased our understanding of many related phenomena in the past decade—transplantation rejection, contact sensitivity, and the chemical mediators of tissue sensitivities; histamine, acetylcholine, and/or the slow reacting substances of anaphylactic shock; as well as lymphocyte-derived soluble substances of delayed hypersensitivity. These latter factors include: transfer factor, migration inhibition factor, chemotactic factor, lymphotoxin, blastogenic factor, interferon, cytotoxic factors, and immunoglobulins, among others (86, 87). The reactions of sensitized lymphocytes with their specific antigen elicit the production of substances involved in inflammatory responses. Employment of biological in vitro tests to indicate the release of such factors or responses has been used as indirect evidence that cellular immunity is involved in the disease process. For example, specific alterations of peripheral leukocyte migration reported to be due to the production of the migration inhibition factor, can be induced in the presence of antigens extracted from target organs in ulcerative colitis (88), glomerulonephritis (89), and thyroiditis (90).

Lymphocytes from sensitized animals react to antigen in vitro with increased blast transformation and increased DNA synthesis via the blastogenic factor when compared with normal controls. Incorporation of H^3-thymidine in the presence of phytohemagglutinin stimulation is used in these assays (87).

Housley and Oppenheim in 1967 were the first to utilize these principles to study lymphocytes from myasthenic patients. They reported that lymphocytes of both thymectomized and nonthymectomized myasthenic patients respond equally well to phytohemagglutinin stimulation as measured by DNA synthesis and by blast formations (91). However, they found no changes in response to thymus or muscle antigen stimulation. Neither toxicity curves nor proteins were measured in this study. Since muscle antigens such as myosin are very labile, it is also possible that the potency of their antigens had changed in preparation or storage. Saunders et al, however, were able to show good lymphocyte stimulation with human muscle homogenates in 8/11 patients with polymyositis (92). Unpublished data from our laboratory would be in agreement with this latter study.

In 1969, Namba et al reported that lymphocytes of myasthenic patients cause a more severe systemic graft-versus-host reaction in mice than do normal human lymphocytes (93). Motor endplates also showed a marked increase in mean diameter accompanied by changes in fine structures as well as local inflammatory reactions in the muscle per se. These changes were more marked after injection of myasthenic lymphocytes as compared to normal control lymphocytes. Electronmicrographs have shown elongation of motor endplates in biopsies obtained from patients with myasthenia gravis similar to those found in more primitive embryological endplates (9) (see section on neurology).

Koster et al have demonstrated that sensitized rat thoracic duct lymphocytes formed during an acute Listeria infection can move into exudates produced by any variety of inflammatory stimuli (94). There seems to be an affinity of sensitized cells for any inflammatory focus.

Conversion of Candida albicans from commensalism to pathogenicity was reported in a patient with myasthenia gravis where thymoma was present (95). While association of thymoma with agammaglobulinemia has been described (96), this is the third case of its kind reported where normal globulins were measured. The authors speculate that thymoma may have induced production of defective lymphocytes or inhibitors of one or more of the soluble mediators of cellular immunity. Chilgren had previously postulated that in these patients the afferent pathway of cellular immune responses was intact but that migration inhibition factor was either present in inadequate amounts or was blocked (97).

Transient states of anergy are found in certain viral disease of man which are associated with absolute leukopenia but relative lymphocytosis, namely, rubeola, rubella, influenza, infectious mononucleosis, varicella, and poliomyelitis. It is conceivable that temporary anergy results from the capacity of virus to invade the reticuloendothelial system and to interfere with its normal immunologic function. An experimental animal model of viral-induced anergy has recently been reported (98).

Recent investigation of Kveim-positive sarcoidosis patients suggests that responsiveness to Kveim antigen may preempt production or function of "memory cells" for delayed hypersensitivity to other antigens. Blaese et al recently studied recruitment of anergic patients' lymphocytes for cell-mediated cytoxicity by specific antibody (99). Three functions of lymphocytes were shown in vitro: response to antigens; reactions with allogeneic cells; and cell interaction with human serum antibody-mediated cytotoxic reactions. They demonstrated that anergic patients may be deficient in one or more of these classes of lymphocytic activities.

An anergic condition exists to an even greater extent in Hodgkin's disease (100). It is probably caused by a lack of sufficient immunocompetent cells capable of engagement by transfer factor to initiate a local reaction. Churchill et al studied lymphocyte function in patients with Hodgkin's disease in vitro utilizing migration inhibition, mitogenic activity, and response to tuberculin protein (PPD). Twenty out of 24 patients had lymphocytes that produced at least one of these mediators. This strongly suggests that impairment of delayed hypersensitivity may be due to defective production of one or more mediators or perhaps due to defective function of cells other than lymphocytes. Studies by Louie and Goldberg, indeed, suggest such a combined cellular defect (101). In their study, lymphocytes were unable to respond to specific antigen, and patients' monocytes showed a relative insensitivity to migration inhibition factor (MIF). In considering the relationship of anergy to autoimmune etiology, many factors and levels of interaction may possibly be involved.

Several phenomena had suggested to us that cell-mediated immunity might be involved in myasthenia gravis. These included the fact that remissions in myasthenia gravis often followed removal of the thymus—an organ related to the development of lymphocytes which recognize foreign and self antigens. In myasthenia, the persistence of thymus, as well as the presence of germinal centers are often evident (102). Lymphorrhages in or near muscle also suggested that cell hypersensitivity to muscle should be measured (6).

The direct migration inhibition technique of Søborg and Bendixen was utilized (103). Peripheral lymphocytes from patients with myasthenia gravis and from normal controls were used to measure their reaction to nontoxic crude muscle antigens. Actomyosin and myosin prepared according to the methods of Kielly and Bradley were compared with crude muscle extracts in these assays (104). The migration inhibition technique has been shown to correlate well with in vivo delayed hypersensitivity to such antigens as brucella (105) and tuberculoprotein (106). It has been used successfully to demonstrate cellular sensitization to intestinal antigen in ulcerative colitis (88) and to mitochondrial antigen in Hashimoto's disease (89). Rosenberg and David (107) have recently modified the original technique to permit reliable use of a soluble antigen preparation.

Results reported from our laboratory by Alpert, Rule, and Osserman indicated that significant inhibition of myasthenic peripheral lymphocytes occurred in 14 out of 21 cases (108). While the mean migration index reported for normal controls was 1.08, the mean value reported for myasthenics was 0.68 ($P < 0.01$). Although crude muscle extracts and actomyosin were utilized at similar concentrations, fresh myosin preparations could be used at one-twentieth of these concentrations (10 μg) to obtain the same results. These data were of particular interest since Ricken's experiments (56) and those in our own laboratory had indicated that myosin contained the most active antigenic substance in humoral systems (54).

Correlation of the reciprocal of antibody titer by indirect immunofluorescence with migration inhibition showed that those patients with significant indices (<0.75) also had significant titers of circulating antibodies ($>1/125$). Those patients whose cells had insignificant migration indices (>0.75) also had insignificant antibody titers ($<1/30$). Only four out of 24 patients had significant migration indices to muscle without antibody titers of note. But no myasthenic patients had humoral immunity without cell-mediated immunity (108). These data suggest that the presence of lymphocytes sensitized to muscle antigens may be more important than the presence of circulating antibodies in this disease.

The possibility that both work in concert to provoke autoimmune injury or lessened muscle reactivity locally cannot be excluded. Unpublished data indicate that the presence and extent of muscle lymphorrhages found at autopsy correlate well with antibody titers. Rapid increases in antibody titers have previously but inconsistently been related to activity of clinical disease. Thus, the concept of local immune injury in myasthenia gravis is not illogical (109).

Sensitized lymphocytes in proper ratio can kill specific target cells in culture. Specific cytotoxicity depends upon the cell-bound antibody on lymphocyte cell membranes (110) which causes them to adhere to target cells. It is not complement-dependent. It can be inhibited by previous treatment of target cells with humoral antibodies. These cover antigenic sites on target cells, thereby preventing their reaction with the sensitized lymphocyte. Development of this cytotoxic property is stimulated by contact with antigen on the surface of the target cell. Similar cytotoxicity by previously nonsensitized lymphocytes for cells in culture has been shown to result from stimulation induced by nonspecific agents such as phytohemagglutinins. The only prerequisite for cytotoxicity by lymphocytes appears to be modification of the lymphocyte by agents which induce blast transformation and close contact with antigen on the surface of the target cell.

Following our report in 1971, Armstrong et al recently reported an in vitro study of thymic cells and circulating lymphocytes in five patients with myasthenia gravis (111). These cells showed similar rates of transformation in response to phytohemagglutinin, antilymphocyte globulin, concanavalin A, and tuberculin. There was no difference between these results and those obtained on circulating lymphocytes from normal controls. While normal thymus cells did not produce cytotoxicity, PHA stimulation of thymus cells from a case of myasthenia gravis caused marked destruction of muscle cultures. In agreement with our studies, thymic cells from patients with myasthenia gravis showed migration inhibition with specific antigens, including muscle.

The continued interaction both of the chemical and the soluble factors of delayed hypersensitivity on the polarization of muscle membrane warrants further investigation. Excitation of the membrane at the postsynaptic acetylcholine receptor site may be altered by histamine or the slow reacting substances of anaphylactic shock. The ability of antibodies to lessen membrane potentials has previously been noted (112). The effects of sensitized lymphocytes on membrane potentials remains unknown.

Cellular sensitivity to self antigens need not reflect a primary immunologic process but a response to injury initiated by other factors. Nevertheless, the role of cell-mediated immunity to muscle components in conjunction with circulating antibodies in the perpetuation of myasthenia gravis warrants further investigation.

Immunosuppressive Therapy

Adrenocorticotrophic hormone (ACTH). In many autoimmune diseases such as rheumatoid arthritis, polymyositis, systemic lupus erythematosus, and periarteritis nodosa, use of corticosteroid therapy can increase muscle strength. Both antiinflammatory and immunosuppressive mechanisms may be presumed to be involved. Prolonged administration of steroids results in severe muscle weakness and wasting. However, in myasthenia gravis, a unique set of reactions occur. A rapid decrease in muscle strength usually occurs within the first 3 to 5 days of treatment with 100 U ACTH-gel per day. Muscle strength returns rapidly 3 to 5 days after completion of treatment (113, 114).

Studies in our laboratory indicate that while humoral antibodies may be significantly lower during period of ACTH treatment, they usually return to approximate pretreatment levels at time of clinical improvement. Peripheral lymphocytes sensitized to muscle elicit similar migration inhibition responses both before and during ACTH treatment. Preliminary studies in our laboratory suggest that if significant improvement of myasthenic symptoms occurs after ACTH treatment, inhibition of lymphocyte migration in presence of muscle antigens is significantly decreased or disappears. Potential role of membrane alterations in the rapid improvement after termination of ACTH treatment has not been defined.

The pituitary-adrenal axis has been shown to be intact in myasthenic patients (115). A ten-day course of methylprednisolone produces essentially similar effects to a ten-day ACTH course (116, 117). The ineffectiveness of metapyrone implies that the action of ACTH is mediated via the adrenal cortex (115).

Desoxycorticosterone administration aggravated myasthenic weakness in 10/13 patients and improved muscle strength in 2/13 patients while one patient remained unchanged. The administration of aldosterone to two patients produced marked alterations in water excretion and in serum and urine electrolyte levels without affecting muscle strength (117). Although increased aldosterone secretion has been observed in ten myasthenic patients during clinical exacerbations, mineralocorticoids have no appreciable effect on the disease and hence do not appear to be the mediator of ACTH action.

Boshes has shown that large doses of ACTH can produce neuromuscular block in experimental animals (118). Other investigators have failed to discover a direct action on neuromuscular transmission in either myasthenic patients or in rats following closed intraarterial injections of ACTH or prednisone. A direct corticotrophic effect on motor endplate membrane-causing alterations in the Na^+/K^+ pump or competitive inhibition at receptor sites cannot be ruled out. Prolonged administration of corticotrophin or corticosteroid B have produced elongation of motor endplates as demonstrated by staining for cholinesterase activity (119). As this was done in rabbits, we cannot be certain that such effects can be transposed to patients with myasthenia gravis.

Increased activity of both true and pseudocholinesterase have been found following administration of ACTH in humans and animals. This observation both agrees and disagrees with observed clinical effects.

One speculation is that ACTH may suppress intracellular diphosphoesterase and thereby allow reaccumulation of cyclic AMP (28). Cyclic AMP is well known to control the intracellular accumulation of ATP, vital to all energy processes in the cell, including active transport of ions and metabolites through the membrane. This could directly affect creatinin-phosphate, ATP, ADP interrelationships that provide energy for muscle contractions, polarization of the membrane or the active transport of choline into the neuron.

Control of many hormone receptor sites on the cell surface is related to the cyclic-AMP system. Unpublished data of Rosenberg et al (personal communication) showed that the synthesis of acetyl + choline into acetylcholine was significantly lower in myasthenic muscle compared to normal controls. Xanthines are known to allow the accumulation of cyclic AMP which may be necessary for conversion of choline into acetylcholine. This would seem to be borne out by the report of a case of a thymectomized myasthenic female who was unresponsive to pyridostigmine and ACTH therapy (28). After administration of large doses of oxtriphylline (choline salt of theophylline), she became ACTH-responsive again and demonstrated marked clinical improvement. The administration of choline alone was without effect. We have not observed improvement in an anticholinesterase unresponsive patient with administration of oxtriphylline.

Clinical observations suggest that ACTH effect is not thymus-dependent, but thymus-potentiated. Prolonged corticotrophin or corticosteroid therapy causes shrinkage of both thymic and lymphoid tissue (113).

While lymphocytes are sensitive to corticotrophin, corticosteroids, and radiation, sensitized lymphocytes are more resistant to such modalities. Clinical and laboratory confirmation of such resistance is in progress. We have not observed significant or persistent lymphopenia either pre- or postthymectomy in a series of ACTH-treated cases.

The following mechanisms have been postulated for immunosuppressive activities of ACTH and adrenocorticosteroids: inhibition of migration of immune complexes through vessel walls, reduction in phagocytic monocytes at reaction site, suppression of lysosome release, interference with the complement system, reduction in germinal center formation, suppression of immunoglobulin levels, and suppression of short-lived lymphocytes. Dosages of ACTH or cortisone sufficient to evoke the above responses do not affect histamine flare, immediate hypersensitivity, humoral antibody response, or previously sensitized lymphocytes to any significant extent (113).

Systemic administration of cortisone and ACTH is known to markedly depress tuberculin sensitivity due to inhibition of mononuclear cell infiltration and creation of a relative lymphopenia. Over a long period of time ACTH blocks in vitro measurements of the soluble mediators of delayed hypersensitivity. Whether this is due to lack of synthesis of these substances or due to refractory target cells is unclear.

ACTH therapy inhibits antibody synthesis and the production of sensitized lymphocytes only when good clinical improvement is seen. Thus, the mechanisms and sites of action of ACTH in myasthenia gravis operate at many levels. Greater understanding of its major mode of operation is needed.

Other hormones. Frequent exacerbation of clinical myasthenia in the premenstrual state prompted administration of female hormones for suppression of ovulation with some benefit in our clinic. Testosterone alone was of no value in males. However, administration of testosterone with estrogen in males gave clinical benefit. There have not been adequate studies of pituitary-ovarian or testicular axes to permit any statement concerning the mechanism of such hormone action.

The predilection of this disease for females, as well as the effects of pregnancy on this disease have also raised the specter of specific endocrine influences. Serum IgG levels during pregnancy or in presence of chorioepithelioma bear an inverse relationship to human gonadotropin levels and absolute lymphocyte counts. If effective chemotherapy is given in malignant trophoblastic disease, the above finding can be reversed. In two severely ill myasthenic female patients under close observation, weekly administration of 10 cc of human IgG injected intramuscularly in our clinic, favorably influenced the clinical course and the anticholinesterase response over a period of 1½ years.

Several hormones can affect cellular immunity. These include chorionic gonadotropin, progesterone, growth hormone and estrogen. Tuberculin sensitivity is depressed in hypothyroidism. Administration of thyroid extract restores such sensitivity. Thymus atrophy can be induced in young mice by an intraperitoneal injection of rabbit anti-mouse pituitary serum (120). Inhibition of body growth and a wasting syndrome resembling "runting disease" are seen. This antipituitary serum contained antibodies against acidophilic, growth hormone-producing cells of the anterior pituitary. Neonatally, thymectomized mice show marked degranulation in these acidophilic cells, suggesting a pituitary-thymus axis. It has been noted that hereditary pituitary dwarf mice have hypertrophic thymus and lymphoid tissue. The cellular immune response is depressed in hypothyroidism. It can be restored to normal by thyroid therapy, but can be made more sensitive by the induction of clinical hyperthyroidism. It is believed that thyroxin acts on the proliferation of lymphoid cells whereas growth hormone alone or in combination with thyroxin, presumably acts on the maturation process of precursor cells (121).

Hormones act at many levels in myasthenia gravis. Those modalities which affect cellular immunity and/or soluble mediators of delayed hypersensitivity seem to affect the disease most positively. Detailed investigations of the role of the endocrine organs in the normal immune response as well as an autoimmunity should clarify the role of hormones in immunity.

Antilymphocyte serum and related immunosuppressive therapy. Antilymphocyte serum (ALS) inhibits delayed hypersensitivity and prevents allograft rejection in animals (122–124). ALS acts to deplete paracortical lymph node areas where recirculation of antigen-sensitive lymphocytes occurs. Following ALS treatment, germinal center development in lymph nodes is impaired and a plasmacytoid hyperplasia occurs outside the thymus dependent area. Similar results are obtainable with antithymocyte serum (ATS). Prolonged thoracic duct drainage inhibits cellular hypersensitivity (125) and, conversely, thoracic duct lymphocytes from sensitized rats can transfer delayed hypersensitivity reactions.

In 1971, Pirofsky, Reid, et al reported on use of goat antihuman thymocyte globulin (ATP) therapy in eight myasthenic patients over a 28- to 73-day period (126). Varying degrees of clinical improvement were seen in 7/8 patients while one experienced exacerbation of the disease. Serum IgG was elevated in all patients while C'_3 was elevated in 6/8 patients. Primary humoral antibody response to typhoid vaccine was weak and did not persist while secondary response was not suppressed. Primary cellular immunity as tested with DNCB was suppressed in two thymectomized patients. Response to intradermal skin tests with trichophytin, candida and mumps antigens was only partially inhibited. Rejection of skin grafts was delayed in all patients. Several patients developed antigoat antibodies, and one patient had a mild anaphylactic reaction. These reactions can be markedly reduced if large doses of steroids or aziothioprene are given concomitantly with ATG. Previous thymectomy seemed to enhance probability of clinical improvement with ATG treatment. This correlated well with slower graft rejection and suppression of primary and secondary immune responses.

Intact antilymphocytic gamma globulin molecules are capable of agglutinating lymphocytes in vitro or causing cell lysis. In vivo ALS produces lymphopenia and produces affects similar to those observed after neonatal thymectomy. ALS can depress or abolish delayed hypersensitivity or contact sensitivity to DNCB and prolongs survival of grafts (127). Although ALS can also diminish humoral antibody production, effects are more related to production of generalized lymphopenia than to specific reactions with thymic dependent lymphocytes (128). It seems that ALS alone or in conjunction with thymectomy can effect a reduction in anamnestic antibody response suggesting an abrogation of "immunologic memory." Other immunosuppressive effects can potentiate the effect of ALS only if given before or close to time of administration of first dose of ALS (127).

It is believed that ALS acts by depleting the pool of immunocompetent lymphocytes. It may also cause immune inactivation by coating the surface receptor sites with ALS antibody (129). This may prevent sensitization by antigen or it may prevent these sensitized cells from attacking susceptible tissue. Immunosuppressive effects of ALS act longer than biologic half life of these molecules. It is possible that a dedifferentiation, or blocking factor, at the RNA-DNA level might also explain these reactions. That ALS stimulates an abortive immune response is unlikely because ALS remains immunosuppressive in animals previously made tolerant to gamma globulin contained in the injection (130).

Thymectomy potentiates effects of ATG and ALG (127). Depletion of thymus-dependent paracortical areas in lymph nodes may be related to its immunosuppressive effects. ATG is often more potent than ALG. This would be in line with the present thought that various antilymphocyte sera react predominantly on long-lived thymic derived lymphocytes (127, 131). Studies in our laboratory have implicated these lymphocytes in myasthenia gravis. With in vitro studies of migration inhibition it seems reasonable to assume that thymectomized patients with myasthenia who show delayed hypersensitivity to muscle antigens should theoretically benefit by ALS treatment.

Some patients with severe myasthenia gravis have been refractory to thymectomy and/or ACTH therapy. Limited use of aziothioprene and other antimetabolites in small series of such patients in the United States has been discouraging (132). A recent report from Hungary with a larger series of patients appeared more promising (133).

A recent study by Perlo et al suggests that radiation prethymectomy lessens the probability of germinal centers postthymectomy (134). Radiation of patients prethymectomy whose clinical and laboratory indications might suggest presence of germinal centers would be of interest. Additional clinical studies with immunosuppressive modalities such as ALS and antimetabolites in the treatment of patients with immunologic forms of myasthenia gravis appear warranted.

The Thymus in Myasthenia Gravis

While the link between thymomas and myasthenia gravis was established early in the twentieth century, the role of the thymus in cellular immunology was only dimly appreciated in 1960 (135). The rationale for the brilliant surgery of Blalock in 1939 and 1944, as well as the series of Keynes in 1946 and 1949, was more fully appreciated in the 1960's (13). The series of thymectomies described by our own group in 1971 fully established the beneficial results of thymectomy and its potential relationship to modern immunology (1).

Studies by Papatestas, Alpert, Osserman, Osserman, and Kark in 1971 suggested a direct correlation between clinical severity of myasthenia and the number of thymic germinal centers (1). They attributed the delayed effects of thymectomy in myasthenia gravis to surviving pools of thymic-derived long-lived lymphocytes sensitized to muscle which die off slowly and gradually. They relate their clinical observations in humans to the results obtained with experimental thymectomy in the adult mouse. Miller, Metcalf, and Taylor reported a depressed cellular immune response after an asymptomatic interval of several months (136–138). Miller suggests that the thymus continues to function in adult life. Its effects are only missed once the pool of immunocompetent lymphocytes has been depleted.

While thymectomy brings about remission in a large percentage of myasthenic patients within eight years, the fact that certain patients will go into remission immediately or within a year suggests that removal of long-lived sensitized lymphocytes may not be the basic factor in disease reversal. Also, thymuses removed from patients vary from those with thymomas, those with germinal centers and/or cell hyperplasias, to those thymuses which are highly cystic, degenerate, or nonexistent (102).

Decline in serum muscle antibodies and rise in complement in myasthenic patients responding to thymectomy suggest that the thymus may have been directly involved in the pathogenesis and/or production of these antibodies. Smiley et al (139) were not able to prove this point. Alpert et al from our laboratory recently analyzed 79 thymuses removed from myasthenic patients (140). No consistent relationship between lymphoid follicular hyperplasia and presence of circulating antibodies to striated muscle was found. Several other studies have also failed to show specific antibody synthesis in thymus cultures.

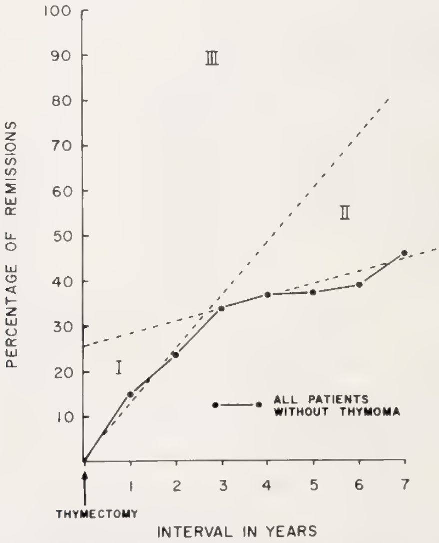

FIG. 2. Percentage of remission and year postthymectomy. I. Rapid recovery, few germinal centers; II. Slow recovery, many germinal centers; III. Nonresponsive to thymectomy.

It is possible that thymocytes whose mitotic index is ten-fold that of unstimulated lymph node cells could produce nonspecific immunoglobulin at the time of rapid DNA replication. Normal thymus, spleen, and lymph nodes have a ratio of immunoglobulin synthesis of 1:6:25 on the basis of C^{14}-labeled amino acids incorporated into immunoglobulin fractions obtained from these organs on a wet weight basis (139).

Smiley et al have shown that thymic tissue obtained from myasthenic patients synthesized six times more immunoglobulin than did normal thymus tissue. In terms of the total soluble protein synthesized, myasthenics produced three times more than the normal thymus. The ratio of IgG:IgA:IgM was 22.1:5.0:1.6% of the total protein produced (139). Their study established that normal as well as hyperplastic thymuses share with peripheral lymphoid tissue the capacity to produce immunoglobulin. These authors found that IgG from neither normal nor myasthenic thymuses reacted with normal or myasthenic thymus or muscle as studied by radioautography and immunofluorescence. There apparently was no correlation between results and presence or absence of circulating immunofluorescent muscle antibodies. Unlike myasthenic thymus, normal thymus synthesized only minimal amounts of IgA and IgM.

Animal observations suggest that the thymus is essential to development of immunologic responsiveness of the cellular type. It is much less important in development of humoral responsiveness. Thymic control of immunologic capabilities continues at a reduced rate into adult life. Lymphocytes in the circulation, the lymphatics, the thoracic duct, and the peripheral nodes develop under thymic influence (141). When H^3-thymidine is injected into the thymus in order to label the contents of the gland, the label is consequently found in lymphocytes of mesenteric nodes, spleen, and Peyer's patches (142). It has also been shown by means of chromosome markers that lymphocytes from thymic grafts also appear in peripheral lymph nodes and spleen (143). After the immediate neonatal period thymic involution begins. The cortex shrinks more rapidly than the medulla although the thymus seems to remain the most active site of lymphopoiesis during early infancy. Neonatal thymectomy in animals sharply reduces lymphocyte contents of paracortical areas of lymph nodes and of periarteriolar lymphatic sheaths of the spleen.

Neonatally thymectomized animals fail to reject skin homografts from donors of foreign strain, even those differing at the H_2 locus (144). Cells from lymphoid organs of such animals are less able to provoke a graft-versus-host reaction after inoculation in appropriate recipients than are similar doses of cells from normal mice. While neonatal thymectomy in mice produces lymphopenia and markedly decreased immune response, serum immunoglobulin levels remain normal.

Thymectomy in man, beyond infancy, causes lymphocytopenia only irregularly and transiently. Its effects on immunologic capacity are likewise variable. Restoration of normal thymic function in thymectomized mice with cell impermeable millipore diffusion chambers containing thymus tissue points to existence of potential immune regulating factors within the thymus (145). In recent studies, injection of thymosin, a soluble semipurified extract of calf thymus, had the ability to reverse runting disease in a significant number of newborn mice (146).

Miller et al suggest that the thymus exerts its influence on development of precursor antigen-sensitive cells. Once such clones have been produced, the thymus is no longer needed. Postthymectomy wasting in animals has been prevented by infusion of thymocytes or lymphocytes obtained from lymph nodes, spleen, or thoracic duct. Fetal liver cells and bone marrow cells did not reconstitute immunologic capacity of neonatally thymectomized mice. Immunocompetent thymocytes were necessary to prevent death while thymic stroma induced competence in host precursor cells. The longer the delay in thymus grafting after neonatal thymectomy, the less probable was immunologic restoration. Thus, host lymphocytes responding to such grafts presumably were initially under thymic influences (143). Existence of an intact thymic reticulum is required to give rise to normal epithelial cells. The finding that bone marrow cells, unlike thymocytes or peripheral lymphocytes, can repopulate the thymus of lethally irradiated animals suggests that bone marrow cells may have a special attraction for "homing in" on the thymus (147). Recent work by Winkelstein has shown that mixed cell cultures of thymus and marrow lymphocytes can act synergistically to generate increased numbers of PHA responsive cells (148).

Yunis et al have shown the existence of partially differentiated cells which are insensitive to thymic hormone but require contact with the thymus gland in order to become fully immunocompetent (149). Such "postthymic cells" increase in number after birth and escape into peripheral lymphoid tissue.

Relationship of the thymus to autoimmunity in man is related to pathologic thymic changes in such autoimmune diseases as systemic lupus erythematosus, rheumatoid arthritis, rheumatic fever, scleroderma, thyroidtoxicosis, Sjögren's syndrome, glomerulonephritis, aplastic anemia, and myasthenia gravis. Major clinical observation is the association of germinal centers in the thymus. These are usually not observed in a normal population. High coincidence of thymoma with myasthenia gravis in about 10 to 15% of patients is well known. Thymomas have also been reported in patients with systemic lupus erythematosus, Sjögren's syndrome, and agammaglobulinemia. It is not clear whether the thymomas found in erythroblastopenia are truly autoimmune in nature (150).

Genetic susceptibility to autoimmune disorders exists in animals. Its high incidence in families of patients with immune deficiency diseases suggest that certain inherited predispositions exist in humans. The NZB strain of mice is the best autoimmune animal model (151). After three months of age these animals regularly develop hemolytic anemia, positive Coombs' tests, antinuclear antibodies, thymic hyperplasia with germinal centers, and a deficiency of adult type of epithelial cells in the thymic medulla. Decreased ability to yield delayed hypersensitivity reactions is also found. Aging NZB mice showed deposition of anti-DNA complexes in the kidney and had a high incidence of lymphoid malignancy and amyloidosis.

Neonatal thymectomy in mice is followed by: a. accelerated appearance of antinuclear antibodies in autoimmune susceptible strains but to a lesser degree in autoimmune resistant strains; b. marked anemia; and c. histiocytic and plasma cell infiltration of lymph nodes. In vitro tests on aging NZB autoimmune susceptible mice suggests a progressive quantitative or functional loss of postthymic cells (149).

Mellors et al have suggested a linkage between the Gross leukemia virus and autoimmune and/or malignant factors in NZB mice (152). It is known that viruses per se can be immunosuppressive (vide supra). Aging, thymic involution, and genetic factors in concert with virus could overwhelm the thymus and/or thymic derived cells. A thymus-deprived system could conceivably be overwhelmed by infections while the humoral antibody system could be excessively stimulated by foreign antigens. Under such conditions foreign antigens may cross-react with an animal's own antigenic constituents and not be recognized. Local inflammatory reactions could also cause initiation of antibody synthesis to self components. It has also been observed that autoimmune resistant strains of mice may develop autoantibodies after thymectomy. Genetic mechanisms may also control involution of thymic dependent cells during aging (151).

The importance of cellular immune mechanisms in human cancer has been observed by many investigators. Patients with congenital immunologic deficiencies; those on extensive immunosuppressive therapy; and those with chronic lymphocytic leukemia, all carry an increased risk of malignancy. It has also been demonstrated that prolonged survival in Burkitt's lymphoma varies directly with the ability to yield a positive delayed hypersensitivity reaction to the tumor antigen (153). Similarly, thymectomy has been shown to elicit a higher probability of malignant response in NZB mice (151), but a beneficial effect in animals bearing spontaneous mammary adenocarcinoma (154) or in mammary tumor virus-induced noduligenesis (155). In our own laboratory Papatestas et al have suggested that thymectomy in a myasthenic population reduces their higher probability of acquiring cancer to that of the norm for their age and sex distribution (3). These findings await further confirmation.

The above discussion emphasizes the relationship of thymic germinal centers to remission postthymectomy in humans, increased production of nonspecific immunoglobulin in thymus glands obtained from myasthenic patients and the appearance of antinuclear antibodies and cancer in the experimental NZB mice. While antinuclear antibodies are present in 22% of our myasthenic population no correlation between germinal centers and the probability of cancer has been noted (82). However, survival of myasthenics postthymectomy appears to be inversely related to presence and extent of germinal center hyperplasia. Occasional permanent complete remission seen after thymectomy and lessened probability of cancer might suggest the removal of a focal unit in patients with myasthenia gravis.

Thus, the thymus appears to play an important role in myasthenia gravis. Whether this role is primary or secondary awaits further investigation.

Hypotheses of the Pathogenesis of Myasthenia Gravis

Myasthenia gravis remains a disease of unknown etiology. The preceding biological background leads to the formation of certain hypotheses of disease pathogenesis as well as to contradictory biologic phenomena. The following hypotheses attempt to present potentially interrelated concepts for current and projected avenues of research. Hopefully they will lend themselves to in vivo and in vitro experimentation.

A mutagenic agent, possibly of viral origin, invades the reticuloendothelial system lodging mainly in the thymus and thymic derived cells. Alterations in the normal DNA-RNA interactions produce abnormal proteins, most probably immunoglobulins. While these changes do not interfere with the ability of the body to combat infections or produce humoral antibodies, these changes are related to the alteration of specific receptor sites for "self recognition" on the surface of thymic-derived cells. Immune surveillance is incompetent to cope with these cells due to anergy produced by the same mutagenic agent. These specifically sensitized lymphocytes then interact with the specific target tissue. In myasthenia gravis this target conceivably may be either muscle and/or motor endplate components. These lymphocytes produce local immune damage and initiate concommitant production of humoral antibodies to the target organ. Antibodies in conjunction with sensitized lymphocytes interfere with production of acetylcholine, the interaction of acetylcholine with its receptor sites and/or its release. As more thymic-derived lymphocytes become sensitized to the "target antigens," the thymus hypertrophies and produces germinal centers to provide more "committed lymphocytes" to the periphery. A vicious cycle is thus initiated.

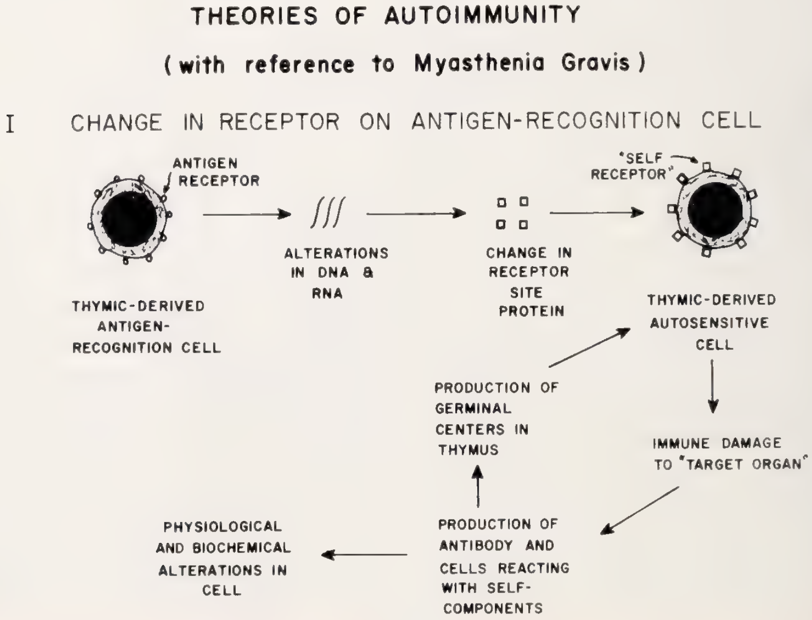
THEORIES OF AUTOIMMUNITY
(with reference to Myasthenia Gravis)
I CHANGE IN RECEPTOR ON ANTIGEN-RECOGNITION CELL
ANTIGEN RECEPTOR
THYMIC-DERIVED ANTIGEN-RECOGNITION CELL
ALTERATIONS IN DNA & RNA
CHANGE IN RECEPTOR SITE PROTEIN
"SELF RECEPTOR"
THYMIC-DERIVED AUTOSENSITIVE CELL
IMMUNE DAMAGE TO "TARGET ORGAN"
PRODUCTION OF ANTIBODY AND CELLS REACTING WITH SELF-COMPONENTS
PRODUCTION OF GERMINAL CENTERS IN THYMUS
PHYSIOLOGICAL AND BIOCHEMICAL ALTERATIONS IN CELL

Fig. 3a.

An alternate immunologic hypothesis for the etiology of myasthenia gravis would involve the peripheral invasion of the muscle or endplate by infectious agents. This invasion would trigger a local inflammatory response resulting in muscle degeneration. Mononuclear cells attracted to this area would then ingest altered muscle or nerve proteins. This would lead to the sensitization of lymphocytes which would initiate both cellular and humoral immune mechanisms. These lymphocytes and antibodies could also cross react with thymic "myoid" cells which might cause the appearance of thymic pathology as a secondary event.

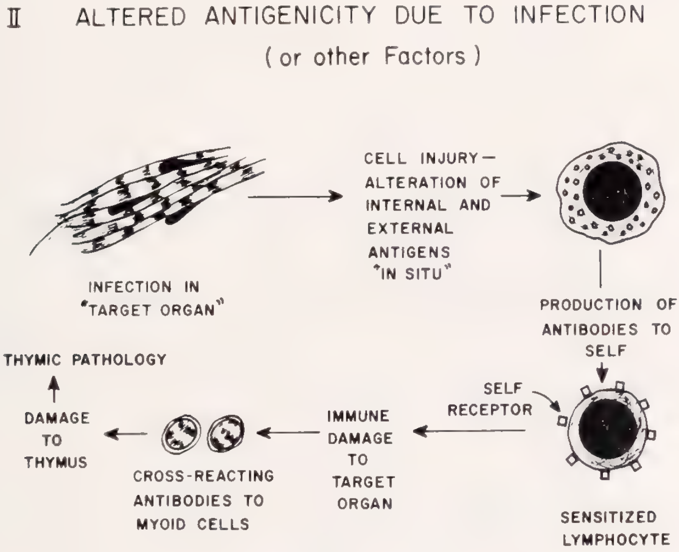
II ALTERED ANTIGENICITY DUE TO INFECTION
(or other Factors)
INFECTION IN "TARGET ORGAN"
CELL INJURY— ALTERATION OF INTERNAL AND EXTERNAL ANTIGENS "IN SITU"
PRODUCTION OF ANTIBODIES TO SELF
SELF RECEPTOR
SENSITIZED LYMPHOCYTE
IMMUNE DAMAGE TO TARGET ORGAN
CROSS-REACTING ANTIBODIES TO MYOID CELLS
DAMAGE TO THYMUS
THYMIC PATHOLOGY

Fig. 3b.

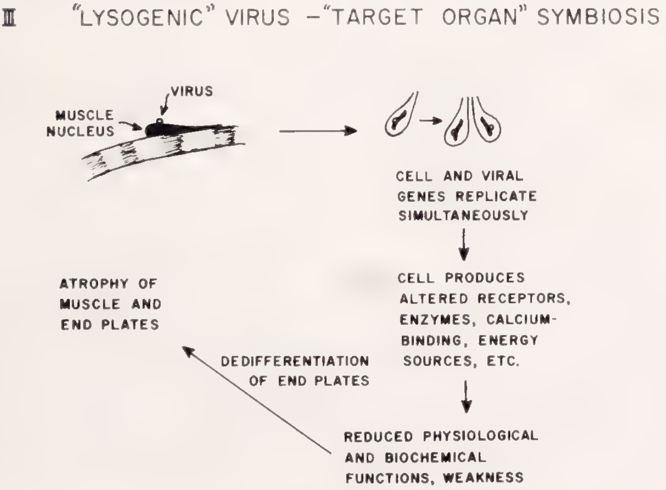
III "LYSOGENIC" VIRUS –"TARGET ORGAN" SYMBIOSIS
VIRUS
MUSCLE NUCLEUS
CELL AND VIRAL GENES REPLICATE SIMULTANEOUSLY
CELL PRODUCES ALTERED RECEPTORS, ENZYMES, CALCIUM-BINDING, ENERGY SOURCES, ETC.
REDUCED PHYSIOLOGICAL AND BIOCHEMICAL FUNCTIONS, WEAKNESS
DEDIFFERENTIATION OF END PLATES
ATROPHY OF MUSCLE AND END PLATES

Fig. 3c.

The above mechanisms do not exclude the possibility of either a simultaneous or independent lysogenic or symbiotic phase of viral infectivity in either thymus and/or muscle. Integration of the viral and host genome would not lead to production of viral particles. However, the invasion of muscle and/or peripheral neurons by such an infection would produce a nonimmunologic form of myasthenia affecting both pre- and post-synaptic nerve transmission and subsequent contractile events. This would occur by evoking changes in surface receptors, by qualitative and quantitative enzyme changes, by alterations in intercellular calcium levels and/or different high energy compounds by production of viral-type rather than host products. All of these could affect acetylcholine metabolism and effectiveness. Clinical fluctuations in the course of myasthenia might then be explained by the reversion of an infectious and/or immunologic form of myasthenia to a symbiotic intracellular viral form and vice-versa.

Conclusions

I. Clinical improvement in myasthenia gravis has occurred with pharmacological advances in anticholinesterase administration. Laboratory studies on pre- and post-synaptic mechanisms in myasthenia gravis as well as observations on the variety of morphological changes in muscle-nerve interaction cannot coherently explain the initiation, etiology or spontaneous remissions found in myasthenia gravis.

II. Thymic abnormalities are common in myasthenia gravis. It has not been established whether thymic pathology in this disease is a primary or secondary event.

III. Both thymectomized and nonthymectomized myasthenics are able to combat infection. The duration of the secondary humoral responses seems to be lessened in the thymectomized group. Studies of longer duration paralleling the period of normal thymic involution are necessary.

IV. A majority of myastenic patients respond favorably to thymectomy within seven years. Within the thymectomy-responsive group, two subpopulations may be discerned:

> A. *An immunologic form of myasthenia.* At some point in the onset or progression of this disease, both humoral antibodies and sensitized lymphocytes are found which react with skeletal muscle. It is again unclear whether this represents a primary or secondary event. The presence of antibodies to muscle alone may only be symptomatic of past immune stimulation. However, antibodies in conjunction with sensitized lymphocytes may have the ability to severely alter both the biochemical and physiologic processes of nerve conduction and muscle contraction, whatever the initial stimulation of these phenomena may have been.
>
> Thymectomy alone or in conjunction with immunosuppressive therapy enhances the probability of remission in this immunologic form of myasthenia. Delayed remissions postthymectomy suggest that long-lived lymphocytes may be operative in approximately 20% of patients thymectomized. While the thymus may or may not be of primary etiologic

significance, once stimulated, a self-prepetuating immunologic role ensues.

B. *A nonimmunologic form of myasthenia.* Circulating antibodies and sensitized lymphocytes are not present at time of or prior to thymectomy. There seems to be a correlation between a relative paucity of germinal centers and early remission. This suggests lower or nonexistent levels of immunologic activity in these patients, approximately 30% of those thymectomized. Removal of a focal unit might be suspected.

V. A group of patients exists which has a poor prognosis due to the presence of thymoma. In addition, a very small group of myasthenics exists which is unimproved or made worse by thymectomy. Not enough data exist in this latter group.

VI. The de novo appearance of myasthenia gravis postthymectomy poses many questions. Did a subclinical myasthenia exist prior to thymectomy? Was all thymus tissue removed? Was a protective factor related to immune surveillance eliminated? Available data are unable to resolve these questions.

VII. All patients of all groups have a transient suspension of myasthenic symptoms and anticholinesterase drug requirements postthymectomy.

VIII. Studies on potential viral mechanisms involved in human autoimmune diseases and neoplasias would clarify similarities and differences between humans and currently accepted animal model systems.

IX. Since our suggested hypotheses do not exclude the possibility of other pathogenetic mechanisms, it is our belief that myasthenia gravis should be considered a disease syndrome with autoimmune implications.

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Contributions of the Intensive Care Unit in the Care of the Myasthenia Gravis Patient

CHRISTOPHER W. BRYAN-BROWN, M.D.

During the year 1970–71, forty-five patients with myasthenia gravis were admitted to the Intensive Care Unit (ICU) of The Mount Sinai Hospital. Twenty-nine patients entered the unit postthymectomy, two by means of thoracotomy (1), the rest by the transcervical technique (2). Other reasons for referral were ACTH therapy in five patients, incidental surgery in four, and respiratory difficulties in seven. This paper will discuss the contributions that the ICU has made in the care of these patients and the projected changes for improvement in their treatment.

Respiratory Care

The most precarious situation the myasthenic patient faces is ventilatory inadequacy due to weakness of the respiratory musculature. His airway may be endangered by insufficient power to coordinate swallowing, and he may choke. The feeble cough may be insufficient to clear the airways either of foreign bodies or secretions. Death may occur due to unavailability of trained personnel to establish an immediate airway and provide ventilation. The severely afflicted myasthenic needs continuous and compulsive respiratory care. This is discussed under five headings: monitoring; chest therapy; artificial ventilation; tracheostomy; and control of infection.

Monitoring

Respiratory data are collected routinely on all myasthenics. These patients usually have a tracheostomy which enables accurate measurement of ventilation. This is less possible with a face mask, because air leaks are usually present. Routinely, a Wright respirometer is used. Tidal volume (V_E), minute volume ($\dot{V}$), vital capacity (VC), and respiratory rate (f) are charted. Data are recorded on all patients, whether breathing spontaneously or receiving artificial ventilation. Tidal volume and vital capacity are recorded prior to and immediately after administration of edrophonium (Tensilon®) testing. The Wright respirometer underreads grossly with weakly expired low tidal volume (3), an error on the side of safety. It is not uncommon for a normal-sized patient to have a recorded tidal volume of 150 ml, and show no other signs of respiratory failure. Serial blood pressure determinations may, however, give early evidence of functional anoxia.

Blood gases are not particularly useful in assessment of respiratory failure in the myasthenic, unless there is pulmonary disease. By the time the blood gases are abnormal, the patient is often apparently in distress. The usual pattern in

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From the Departments of Anesthesiology and Surgery, Mount Sinai School of Medicine of The City University of New York, N.Y. 10029.

development of respiratory failure is first a lowering of the arterial P_{CO_2} to levels of 30–35 mm Hg. The P_{O_2} is slightly reduced to around 70 mm Hg. If the patient is now given oxygen-enriched air to breathe, blood gases may return to normal levels with a raised alveolar-arterial oxygen gradient ($D(A\text{-}a)O_2$). The patient may now be temporarily improved, without a hypoxic drive to respiration. An indication that severe acute respiratory failure is imminent is a rising P_{CO_2}. A normal value (40 mm Hg) may give rise to concern if previous values were lower and the patient has poor ventilation.

Upon admission all patients routinely have blood drawn for arterial P_{O_2}, P_{CO_2}, pH, base excess, and hematocrit in order to establish baseline data on acid-base status and oxygen-carrying capacity of the blood. The blood gases remain the determining factor of adequacy of gas exchange and are closely followed on a ventilated patient. Occasionally, to avoid repeated arterial puncture, end-expiratory ("alveolar") carbon dioxide concentration is measured with a continuous P_{CO_2} meter. This is adequate for managing the ventilated patient with healthy lungs, but it requires bulky apparatus and bedside calibration. The nursing staff has no trouble performing this function. Some more repeatable form of measurement of respiratory strength is being considered for the future. Inspiratory effort seems to hold the most promise because it is least affected by the psychological overlay which greatly alters vital capacity in the disturbed patient.

Chest Therapy

The main concern of the doctor caring for the critically ill myasthenic patient is that the lungs are kept in good working order, well expanded, ventilated, and free from infection. This effort at times requires two attendants. One should examine the patient to determine areas of the lung which have poor air entry or that are loaded with secretions. Well-aerated, well-expanded lungs are less prone to atelectasis and serious infection. The weak patient lying on his side will expand the upper part of the lung to a functional residual capacity approaching that found in the standing position (4). Most of the ventilation and pulmonary circulation is in the lower part of the lung. Whenever possible, the patient is fully turned from side to side every two hours. This helps to keep the lungs expanded and aids the passage of bronchial secretions up the now horizontal trachea. If the patient is troubled by retention of sputum, the semi-prone position will give the trachea a downhill route for expectoration. To further help drainage of posterior basal secretions, the patient is sometimes placed in postural drainage for up to twenty minutes. The bottom half of his body is kept prone on the bed, with arms and head resting on a pillow on the floor. Secretions may be further loosened with percussion and vibration, frequently made more effective by inflating the patient's lungs more fully with a resuscitation ("Ambu") bag in an effort to simulate a cough.

Normally, bronchial secretions of the myasthenic patient are easily removed with suctioning. These secretions are kept moist by the bronchorrhea produced by anticholinesterase therapy. They may be aggravatingly copious, requiring cautious use of atropine. To avoid crusting, secretions are usually kept moist by the administration of a mist from a compressed gas nebulizer, or if the patient is being ventilated, by a hot water humidifier. A patient with heavily infected thick secretions may have them liquefied by an ultrasonic nebulizer (De Vilbis), but these are used sparingly because of the risk of contamination and infection (5). Five milliliters of saline may be injected at the time of endotracheal suction. It has not been found necessary to use any mucolytic or other sputum-liquefying agents in myasthenic patients.

Suctioning of patients with secretions is done as necessary, at times every few minutes. The nursing staff is instructed not to damage the tracheobronchial mucosa by vigorous suctioning when there are no secretions. In the ICU, frequency of suctioning is usually determined by the nurse at the bedside, who is given much freedom in the choice of technique for obtaining sputum. She may also initiate postural drainage. The well-oriented patient frequently learns when he needs suctioning and provides a useful guide to his own care. Suctioning protocol requires that the operator be sterile-gloved on both hands. One hand is sterile-gloved so that the suction catheter does not become contaminated; the other so that the operator does not become contaminated by the sputum and thereby possibly infect the next patient. Combined suctioning and chest physiotherapy are most effective when performed by two nurses. When tracheobronchial toilette is carried out on a patient in respiratory failure, he is given five minutes of 100 percent oxygen beforehand. By using these techniques, resort to bronchoscopy has been minimized.

Upon admission, chest x-rays are taken routinely, and thereafter as indicated by the patient's condition.

Artificial Ventilation

Most myasthenic patients in the ICU have at some time required use of a ventilator. As the patient gains more experience on a ventilator there is decreased concern that he will be difficult to wean from it when he becomes stronger. Weaning can be a problem because of the fear the patient feels that if he does not have the use of the ventilator, he may not have enough air to breathe; he panics if the ventilator is removed. The ICU procedures cope with this fear well. The patient is surrounded by medical and nursing staff obviously used to taking care of people with this condition. A resuscitation bag is at the head of patient's bed and a ventilator kept beside it. One myasthentic patient, a physician, felt very discomforted when it was suggested that the ventilator be moved from his bedside, although he maintained that he knew he did not need it. A few days previously, his life had been supported by this apparatus for seventy-two hours. Care of the myasthenic who is failing because of shortness of breath involves the most strenuous effort possible to build his confidence in those caring for him. He knows the nature of his disease is capricious and he must rely upon his attendants.

Criteria for artificial ventilation cannot be defined precisely, mainly because of the patient's variable response to hypoventilation. Capacity to breathe can be estimated. Most patients demonstrating a vital capacity above 10 ml/kg should start weaning from a ventilator. If measurements are made with a Wright respirometer, lower values can be accepted. A tidal volume 3–4 ml/kg may be adequate. A quick estimation of sufficiency of respiration can be made by asking the patient to count out loud. If he can count up to "three" he may manage to continue on his own (an average man can count above "fifty"). One patient continued to support himself for half an hour only able to count "one". He did not want to be ventilated, but then gave up the struggle and agreed.

As a gauge blood gases are of less use than the patient's clinical state, but a rising P_{CO_2} is regarded as a sign of imminent complete respiratory failure. The patient usually will show signs of dyspnea and will often ask to be ventilated. When his airway has been checked and secretions removed, he will then be put on a ventilator if he is still in distress.

For all adults with normal cardiopulmonary function the routine is to set a volume-controlled ventilation of tidal volume 700–900 ml, with a respiratory rate of 12–14 per minute, and a 200 ml dead space between the patient and the ventilator. This is so much a part of the ICU protocol that it can be applied by the nursing staff without difficulty. Forty percent oxygen is administered for the initial period of ventilation. After 20 to 30 minutes, blood gases are measured and further adjustment of the ventilator carried out.

When a patient is ventilated, his P_{CO_2} is kept at 35–40 mm Hg; a level of below 30 is considered a cause for concern. It has been found that patients who have been equilibrated to a low P_{CO_2} are very difficult to wean. Usually this is because of the demand put upon their spontaneous ventilation to keep their P_{CO_2} unnecessarily low. A normal patient requires more than double his minute volume to maintain a P_{CO_2} of normal (6).

To keep the lung well expanded during each breath and to retain carbon dioxide, a dead space is added between the patient and the ventilator circuit. Two hundred ml has been found to raise the P_{CO_2} about 10 mm Hg in the average adult. This method has been found far more satisfactory than the "sigh," which is introduced occasionally. [This is of large volume and may expose the patient's respiratory system to undue pressure.] Every 2 to 3 hours the patient's lungs are routinely expanded during chest physiotherapy.

The following case demonstrates some difficulties that arise when a myasthenic patient is given uncontrolled respiration.

Several weeks prior to the current admission, a 67-year-old man was admitted to The Mount Sinai Hospital for thymectomy which was uneventful. He had a history of chronic bronchitis and mild emphysema but was otherwise well, apart from myasthenia. He did not regain full strength and vigor after his operation. On admission and for the next three days he had to be kept continuously on a triggered pressure-limited (Bird) ventilator, despite the fact that he could manage a 2,000 ml vital capacity and considerable minute volume ($\dot{V}$). At this time, he appeared to have adequate strength. When he was made comfortable, he was taken off the ventilator and given air to breathe. He then proceeded to ventilate well and the following data were obtained: Arterial P_{CO_2}, 16.5 mm Hg; minute volume ($\dot{V}$), 16 liters; P_{O_2}, 64 mm Hg; pH, 7.76.

He was given 40 percent oxygen to breathe and in twenty minutes was in acute distress, begging to go back on the ventilator. The following data were recorded: Arterial P_{CO_2}, 23 mm Hg; minute volume ($\dot{V}$), 9 liters; P_{O_2}, 140 mm Hg; pH, 7.65.

He was then made comfortable on an Emerson ventilator and given 40 percent oxygen. The values then taken were: Arterial P_{CO_2}, 14 mm Hg; minute volume ($\dot{V}$), 18 liters; P_{O_2}, 160 mm Hg; pH, 7.80.

Any attempt at lowering the minute volume was met with considerable protest by the patient. A 100 ml dead space was added to the patient's circuit and this was later increased to 200 ml. The P_{CO_2} rose to 19 mm Hg, but the minute volume had increased 19 liters, indicating that the patient was contributing to his own ventilation. He was given a narcotic (Fentanyl®, 0.2 mg IV), and the minute volume gradually reduced without the patient's knowledge to 16 liters. Six hours after admission his arterial P_{CO_2} was 23 mm Hg, and he was comfortable. Six hours later, the patient was asleep and comfortable with an arterial P_{CO_2} of 27 mm Hg and a considerably reduced minute volume. He had been eating and drinking satisfactorily. With further sedation overnight, he was acclimated to a P_{CO_2} of 33 mm Hg. Twenty-four hours after starting his carbon dioxide buildup, he was breathing oxygen-enriched air with no dyspnea. Data at this point were: Arterial P_{CO_2}, 39 mm Hg; minute ($\dot{V}$), 8 liters; P_{O_2}, 204 mm Hg; pH, 7.48.

Soon he was breathing air, registered normal blood gases, and did not require further ventilation.

The chief trouble with a pressure-limited triggered ventilator is that the patient often becomes massively, chronically hyperventilated and is very difficult to wean from the machine. In the ICU, patients with myasthenia gravis are weaned by having increasingly long periods off a nontriggered volume ventilator, with every effort being made to keep the blood gases normal. This is easiest with a volume-controlled ventilator such as the Emerson or Engström. The Ohio 560 or Bennet MAI have also been used with the sensitivity of the triggering device turned down. The Bird ventilator is mainly reserved for short-term use and inhalation therapy.

Tracheostomy

It has been a very firm policy that all myasthenic patients who have respiratory distress or thymectomy have an elective tracheostomy (1, 2). This easily accessible airway makes emergency treatment for respiratory failure, retained secretions, or aspiration available at all times. Some thymectomy patients have the tracheostomy tube removed after 3 to 4 days postoperation, if strength is adequate.

The nursing staff is taught to manage and replace tracheostomy tubes and the staff's assessment of when the tube should be removed is very valuable. At present, if a patient is likely to be ventilated for several days, or if he has a severe chest infection, a Tracheoflex or Portex tracheostomy tube with a floppy cuff is used. A standard Jackson silver tube with inner cannula and latex cuff is adequate for most patients. Obsessive care is taken to keep tracheostomies humidified and thereby prevent crusting of secretions. Tubes are not changed routinely, but only if they give rise to trouble or when a different size is required. Although inner cannulae are cleaned every four hours, the future ICU routine will be every eight hours and as necessary. There is a minimum of treatment to the skin wound. If there are crusts, they are removed with hydrogen peroxide. The area is usually covered with a single layer of Telfa® gauze or plain gauze. Vaseline gauze is discouraged because it tends to make the skin soggy. Care is taken to prevent the ventilator tubing from dragging on the tracheostomy tube.

As a trial, two selected patients who had good tidal volume and vital capacities were admitted to the ICU. Two courses of ACTH therapy were administered uneventfully to one patient without elective tracheostomy. The thymectomy patient developed respiratory failure and needed intubation, requiring tracheostomy on the second postoperative day.

Control of Infection

If there is a tracheostomy or endotracheal tube, most myasthenic patients have a mixed flora growing in their bronchial secretions. They are prone to chest infection. Treatment is aimed at prevention with more vigorous physiotherapy when chest infection arises. Upon admission, bronchial secretions are cultured—this procedure thereafter repeated twice weekly and when indicated. Physical rather than pharmacologic means are tried first and will usually bring an end to fever due to atelectasis or early infection. ACTH patients with infection are more difficult to treat because they often do not exhibit fever or altered leukocyte count. Clinical physical signs and chest x-ray are necessary.

The use of prophylactic antibiotics, generally Ampicillin®, was routine in postoperative care of thymectomy patients. Eight patients were given a prophylactic antibiotic and later three of these required a change to another antibiotic because of reports of resistance in sensitivity studies. Of the remaining twenty-one patients, five were administered antibiotics when chest infection occurred. One of these required a change of antibiotic. No patient developed mediastinitis. This would seem to indicate that prophylactic antibiotics for this operation produce no benefit. It must be noted that those patients receiving antibiotics are those who had the most complicated surgery—e.g., sternal-split—or pneumothorax and hemorrhage.

Postthymectomy Patient

After a brief immediate suspension of drug requirements, patients who have had thymectomy may vary in the postoperative period from complete remission to mild or acute exacerbation of the myasthenic state. As a rule, these patients are highly sensitive to anticholinesterase therapy. This sensitivity has been discussed in the section on clinical experience. Respiratory care is the key to good management. Physiotherapy to the chest is applied at least four times a day. Pain is not a problem unless there has been sternal-split surgery.

Swallowing is often difficult and for the first few days, hydration of the patient is often by intravenous infusion. If a patient cannot swallow in that time, he will be fed a blenderized diet to which is added about 50 to 100 mEq of sodium chloride. The Mount Sinai Hospital's blenderized diet contains only 30 mEq NaCl/liter. The ICU offers the thymectomy patient a safe environment for a possible time of crisis. Myasthenic patients having surgery for other conditions do not seem to have such an upheaval of their myasthenic status and although they may vary in their sensitivity to pyridostigmine, they remain easier to manage.

Summary

During the past year, forty-five patients with myasthenia gravis have been treated in the ICU. Training and orientation of the medical and nursing staff includes the management of critical and routine problems of myasthenic patients. Respiratory care is the key to successful treatment. Discussed are monitoring, chest therapy, artificial ventilation, tracheostomy, and control of infection.

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Some Anatomic Features of the Transcervical Approach for Thymectomy

ALLAN E. KARK, M.D. AND ANGELOS E. PAPATESTAS, M.D.

Removal of the thymus gland by the transcervical technique, a method which we have adopted as a routine in the past three years, has been described in detail elsewhere (1). Increasing familiarity with the surgical approach and the infrequency of operative or postoperative complications have relegated the transsternal approach to large tumors in the anterior mediastinum or to rare complications such as hemorrhage. The reasons for the clear superiority of the transcervical method over the traditional transsternal approach will be emphasized with particular reference to the anatomic features.

Transcervical thymectomy is done electively with the patient stable on his drug dosage. Nearly 10% of the patients had existing tracheostomies because of a previous acute respiratory crisis. Except in one instance in which the stoma had been placed in the suprasternal notch, this has not been an obstacle to the transcervical approach. Preoperative bacteriologic culture and careful cleansing of the trachestomy stoma with protection of the main incision from the stoma have avoided wound or mediastinal infection.

Preanesthetic medication and techniques of induction, and general technical details have been described elsewhere. The essential anatomic features which are to be appreciated in removing these glands are listed below.

A. The thymus arises from the ventral aspect of the third pharyngeal cleft and from the fourth as well. This forms in the neck at the 5 mm embryo stage and then descends distally into the thorax. Thus, remnants of the thymus may be found anywhere along this line of descent from the hyoid bone to the pericardium—respectively, the limits of the third pouch and the level to which it descends; and thymic cysts and thymomas have been removed from these locations. It is well to recall that the inferior parathyroids arise from the third ventral pouch, are displaced downwards by the thymus descent, and lie caudal to the two parathyroids which arise from the fourth ventral pouch and which, therefore, become the superior parathyroids. The inferior parathyroid may lie along the line of thymic descent within the capsule of the thymus or in the structure of the gland itself in the mediastinum.

B. In the infant and the young child, the thymus is proportionately a much larger organ than in the young adult.

C. The gland invariably lies both in the neck and in the mediastinum, superior and anterior. It is this constant cervical location which makes the transcervical operation feasible. Whether this is invariably true in nonmyasthenic patients is not known.

D. Ectopic thymus tissue, when present, has been reported in the neck. In such circumstances the transcervical approach is a distinct advantage.

From the Department of Surgery, The Mount Sinai Hospital and Mount Sinai School of Medicine of The City University of New York, N.Y. 10029.

E. The gland itself is composed of two halves which do not unite in the midline, and each half has an upper cervical part and a lower mediastinal part. It assumes an "H" shape, the "isthmus" lying just above the level of the innominate vein and representing not true thymic tissue but merely connective tissue adherance.

Appearance

The cervical portion particularly has a fleshy, salmon-pink color and consistency which is quite typical and is at least ½ cm to 1 cm in circumference. The other characteristic feature is the lobular appearance of the gland, the fine separations being produced by septa arising from the capsule to be described below. In older myasthenic patients, the mediastinal parts of the lobes tend to become markedly fibrous with fatty infiltration, and the characteristic features are not as obvious as those of the cervical portions which rarely lose their shape, color, or consistency.

Capsule

This fascia is very cursorily dealt with in anatomic texts, although it is an outstanding anatomic feature of the thymus gland, and its presence and importance are analogous to those of the false capsule of the thyroid and prostate glands (Fig. 1). It is essential to keep within this plane for bloodless and complete dissection of the organ. The fibrous capsule or sheath is noted immediately on separating the strap muscles in the lower neck and appears to be a condensation of fascia lying behind the sternohyoid muscles. Whereas the false capsule of the thyroid appears to be a prolongation of the pretracheal

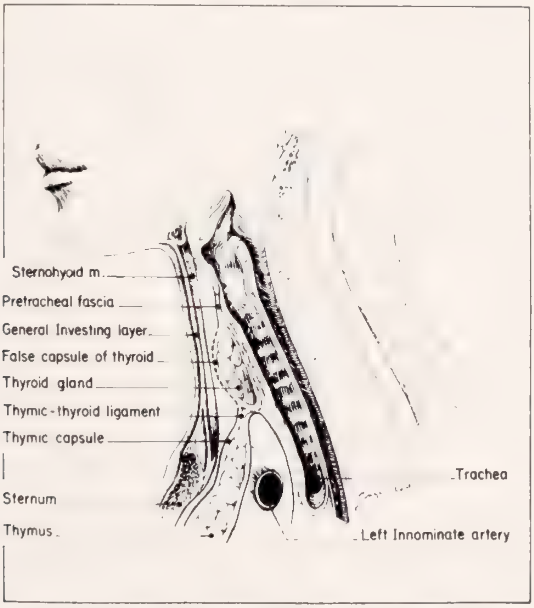

Fig. 1. Demonstrating relationship between thyroid and thymic capsules, position of the thymic-thyroid ligaments, and the well-developed fascial covering of the thymus.

fascia, the thymus at a caudal level lies at an increasing distance from the trachea, and its capsule does not appear to originate from this layer of the fascia. The anterior surface of the upper lobes can be fully exposed and mobilizes only after the division of this fascia by scissors. It will then be seen that the lobe can be pulled out of its ensheathing envelope as a finger is pulled from a glove. The capsule is particularly well developed superiorly where there is a thickening. This has been described in Testut's *Standard French Anatomy Text*, 1930 as thymic-thyroid ligaments (2). The fascia is well developed anteriorly, laterally more so than posteriorly, and needs to be incised by scissors down to the level of the innominate vein. At this level the capsule is strong and especially well developed anteriorly, and it requires careful division to allow traction of the lobes out of the mediastinum. Laterally it is strong as well, and care must be taken to divide the fascia because it is closely applied to the pleura at this point. However, posteriorly where the lobe crosses the innominate vein, the fascia tends to thin out, and in the mediastinum itself it fades away so that the lower lobes can be drawn out without the necessity of dividing it. At this point the fleshy and pink thymus, which in older patients is often infiltrated with fibrous fatty tissue, can nevertheless be clearly distinguished from the yellowish fat of the mediastinum lying on the pericardium. By scissor dissection and occasional clipping of strands of vascular tissue, the lower lobes can, after steady traction be easily delivered. Care is needed at the point where the gland crosses the innominate vein; the pleura is in close contact and may be injured because of traction on it by the fascia. By keeping within the fascial envelope the dissection of the thymus becomes an anatomically precise operation.

Blood Supply and Drainage

The venous drainage of the thymus in most cases is by a single trunk into the anterior or antero-superior aspect of the innominate vein, with two tributaries draining the two lobes. The main trunk can thus be identified easily and carefully ligated. In some cases there are two trunks draining independently into the antero-inferior aspect of the innominate vein, a position which makes for vulnerability and potential danger. The innominate vein should be carefully mobilized by incising its adventitial sheath horizontally for at least an inch so as to make its whole superior, anterior and posterior surfaces accessible and mobile, since the thymic veins, which may enter in a caudal position can only be reached by careful rotation of the innominate vein. Failure to mobilize the innominate vein may result in hemorrhage; on three occasions this has become uncontrollable because the innominate vein which has been twisted during mobilization of the gland resumed its normal position and the inferior opening of the torn thymic vein became inaccessible necessitating a sternal split.

Arterial Supply

Apart from the small arterial twig entering the upper role of the thymus from the inferior thyroid artery, the main arterial supply comes from branches of the internal mammary artery which seldom need individual ligation—a combination of clips or diathermy is adequate for control. Similarly the small vessels near the pericardium do not require specific attention.

Pleural Relationship

The pleural sacs which come together over the pericardium ascend in close proximity behind the sternum in most instances, and in this position come to lie anterior to the thymic lobes, a fact attested to by inadvertent entry into one or other pleural sac when splitting the sternum. However, in many instances the pleural sacs are not so closely applied near the midline and the thymus lies between or even in a slightly anterior plane to the pleural margins. This may occur as a result of lateral displacement of the pleura by the enlarged thymus. At one point in particular the pleural capsule and the innominate vein are in close approximation and care must be taken to insure that what is taken for capsule is not a rotated margin of the innominate vein. Thus, gentle peeling of the capsule with snipping by scissors is necessary, at the same time keeping the pleural membrane away by careful lateral retraction.

Following removal of the thymic lobes the specimen must be carefully laid out on gauze to insure the presence of two upper and two lower lobes in the form of an H. In nearly seventy cases only once was an upper lobe so atrophied as to appear entirely missing and once there was not more than 1 cm of a right lower lobe. These caused enough anxiety to justify a transsternal split for verification. In both instances no evidence of a fully developed lobe was found; in all other cases the four lobes were easily identifiable.

By strong traction of the sternum using a McBurney retractor and good light, preferably fiberoptic, the anterior and superior mediastinum can be completely and easily inspected with lateral view of the parietal pleura which are noted to distend on inspiration without any evidence of puncture. Distal view of the superior and anterior pericardium and particularly the pericardial-pleural sulcus on each side can be thoroughly inspected. This view combined with careful digital exploration insures that no residual thymus remains. On two occasions in which a lobe was found missing on display of the specimen, the remnant which had broken off during dissection at the level of the innominate vein was found easily both on palpation and inspection; in one of the instances the remnant turned out to be a well encapsulated benign 2 cm diameter thymoma which was easily removed.

After closure of the strap muscles and suction drainage the wound is sealed with collodium and a tracheostomy undertaken.

It is of paramount importance that the tracheostomy be done through the smallest possible incision which should be horizontally placed just below the level of the cricoid. An upsetting long-term postoperative feature to patients, particularly young women, is deformity of the tracheostomy which is much more worrying than the well healed transcervical scar which comes to lie just over the sternal notch. It has been found quite satisfactory to have a 1 cm transverse skin incision which can be deepened down to the thyroid isthmus and need not be divided but simply retracted—care being taken to avoid the veins in this area. The second essential feature is to create a flap of trachea by means of an inverted U-shaped incision through the second and third tracheal rings, the lip of which is sutured to the subcutaneous tissue so forming a direct line of entry into the trachea. The importance of this maneuver has been repeatedly confirmed by the need for a replacement of the tracheostomy tube during the early postoperative period when it has inadvertently slipped out or become blocked. Without a flap valve, any eccentricity in placement of the tracheal opening may transform tube replacement into a major undertaking or even make it impossible. In only two instances has nonclosure of a long-term tracheostomy occurred, in each case by epithelialization of the tract. Under local anesthetic, freshening of the tracheal edges and union by catgut sutures is followed by skin closure. The occurrence of a keloid or depressed tracheostomy scar can be handled under local anesthetic by outlining the depressed area, removing the epithelium of the scar, rolling up the scar tissue to form a buttress, and covering it by skin—a technique recommended by Lewin.

Postoperative management of anticholinesterase drugs using the Tensilon® test monitoring and clinical assessment with particular emphasis on vital capacity has been of proven value.

Because of the absence of any significant amount of pain or discomfort the patient can be gotten out of bed and mobilized as soon as muscle strength permits, and the major problem of convalescence is the reinstitution of a stable drug regime. The serious complications of repeated atelectasis, excess secretion, and bronchorrhea are largely induced and aggravated by thoracic cage disruption. Presence of chest tubes has practically disappeared. In a small number of cases the severity of the myasthenia and the unusual sensitivity to drug dosage requiring minimal amounts has meant the maintenance of an unusual degree of muscular weakness. In these cases, inadequate pulmonary expansion has been a problem, but at least it has not been augmented by pain and thoracic immobility resulting therefrom.

The transcervical wound has healed in every case by first intention and wound infection has not been seen despite the fact that in 10% cases a preexisting tracheostomy has been present at operation.

Antibiotics have rarely been used except in the presence of pleura injury and a preexisting stoma.

The late cosmetic results of this incision range from an almost invisible hairline scar to one which becomes a little widened and perfectly acceptable; occasionally there is some keloid thickening. There is no resemblance to the frequent ugly midline sternal scar in young girls which can be quite deforming when keloid or scar depression takes place.

Summary

The immediate postoperative and long term cosmetic advantage of this approach are presented. The anatomic points which form the basis for successful transcervical removal of the thymus are emphasized.

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The Effects of Thymectomy on the Prognosis in Myasthenia Gravis

ANGELOS E. PAPATESTAS, M.D., KERMIT E. OSSERMAN, M.D., AND
ALLAN E. KARK, M.D.

Introduction

Patients with myasthenia gravis have a decreased life expectancy. Comparison of survival curves of patients who have and have not had thymectomy favor the former group (1). A prognostic significance of thymic germinal centers in patients who undergo thymectomy has apparently been demonstrated (2). Myasthenic deaths following thymectomy occurred only in patients with active germinal centers; and a correlation was observed between lengths of survival and degree of activity of the germinal centers.

These thymic lesions are present in 78% of patients with nonthymomatous myasthenia gravis, and have been observed in other autoimmune diseases as well (3). In experimental animals where they occur spontaneously (NZB mice), their incidence varies with sex and age (4). They are viewed by Burnet as manifestation of active proliferation of abnormal clones of immunocompetent lymphocytes (4). In view of the possible role of the latter in the pathogenesis of autoimmune diseases (5, 6, 7) and in oncogenesis (8), the present study was undertaken to evaluate whether, in patients with myasthenia gravis, there is variation in germinal center formation according to sex and age, and whether any correlation exists with the mortality from the disease or with the incidence of extrathymic neoplasms.

Clinical Material and Methods

The records of 1243 patients who have been registered at the Myasthenia Gravis Clinic of The Mount Sinai Hospital between the years 1951–1970 have been reviewed. Two hundred and twenty-six of these patients have undergone thymectomy of which 147 were for the nonthymomatous variety of the disease. Pathology findings at operation in 52 of the latter group have been reported elsewhere (9). The presence or absence of germinal centers was determined in 26 additional operative specimens, and the findings are summarized in Table I. The grading was made on a scale 0 to 4+ in a slight modification of Burnet's scale (4).

Grade	Germinal Centers
0	Absent
1+	Equivocal-Rare
2+	Present
3+	Frequent
4+	Numerous

From the Departments of Surgery and Medicine and The Myasthenia Gravis Clinic and Research Laboratory, The Mount Sinai Hospital and Mount Sinai School of Medicine of The City University of New York, N.Y. 10029.

TABLE I

Thymic Germinal Centers in Patients Undergoing Thymectomy According to Sex and Age

Age (Years)	Males						Females					
	No. Graded	Absent 0	Rare +	Present 2+	Frequent 3+	Numerous 4+	No. Graded	Absent 0	Rare +	Present 2+	Frequent 3+	Numerous 4+
0–9	–	-					1	1	0	0	0	0
10–19	5	0	3	1	1	0	14	4	2	2	2	4
20–19	13	2	6	1	2	2	26	3	5	5	4	9
30–39	1	0	1	0	0	0	13	6	1	1	3	2
40–49	1	1	0	0	0	0	2	0	0	0	2	0
50–59	1	1	0	0	0	0	1	1	0	0	0	0
Totals	21	4	10	2	3	2	57	15	8	8	11	15

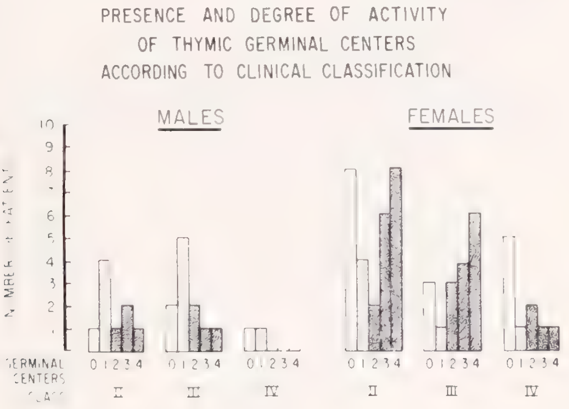

FIG. 1.

Germinal center activity was also determined according to the clinical groups of Osserman's Clinical Classification (10) (Fig. 1). No determination was made in patients with thymomatous myasthenia gravis since residual thymus was available only in a small percentage of cases.

Two hundred and seventy-five of the 1243 patiens have died (22%). Causes of death are summarized in Table II, and the intervals between the onset of myasthenic symptoms and death are shown in Table III.

The total number of extrathymic neoplasms observed in the 1243 patients was 94. Their incidence in the periods prior to and after the onset of myasthenia gravis, and following thymectomy is reported elsewhere (8). The patient-years of observation from the onset of myasthenia gravis to the time of thymectomy, death, loss to/or end of followup, were evaluated separately in each sex and separated into 10-year groups (Table IV). The actual incidence of extrathymic neoplasms in each sex and age group was compared to that expected in a similar group of the general population, using the Connecticut

TABLE II

Causes of Death in Patients with Myasthenia Gravis

Causes of Death	All Patients	No Thymectomy	Thymectomy
All Causes	275	230	45
Myasthenia Gravis	178	139	39
Cause Undetermined	20	19	1
Nonmyasthenic deaths	77	72	5
Extrathymic Neoplasms	28	28	0
Larynx-Bronchus-Lung	5	5	0
Breast	4	4	0
Kidney-Bladder-Prostate	3	3	0
Gastrointestinal Tract-Pancreas	3	3	0
Leukemia	3	3	0
CNS	3	3	0
Ovaries-Uterus-Cervix	2	2	0
Other Extrathymic Neoplasms	5	5	0
Other Nonmyasthenic Deaths	49	44	5

TABLE III

Interval Between Onset of Symptoms of Myasthenia Gravis and Death

Interval in Years	Deaths Due to Mysthenia Gravis		Not Myasthenic Deaths	
		*Ca**		*Ca***
1	46	(7)	8	(2)
2	35	(1)	11	(8)
3	20		4	(1)
4	11		6	(1)
5	16		5	(1)
6	11		2	
7	5	(1)	2	(1)
8	3		4	(1)
9	1		2	
10	5		6	(1)
11–15	8		11	(2)
Over 15	11		11	(5)
Interval not known	6	(1)	5	(5)
All Years Total	178	(10)	77	(28)

* Patients dying of myasthenia gravis that had coexistent malignant extrathymic neoplasms.

** The second column in parenthesis lists deaths due to extrathymic malignant neoplasms.

cancer registry rates for 1963 (7). Corrections for secular time were not made since over 90% of the person-years of observation were distributed in the period 1951–1970.

Direct comparison of the thymectomized with the nonthymectomized popula-

TABLE IV

Incidence of Extrathymic Neoplasm Following the Onset of Myasthenia Gravis and Prior to Thymectomy

Incidence per 10,000 Person-Years of Observation

	Men		Women	
Age Group	Actual	Expected	Actual	Expected
20–29 Years	–	2.6	29.1	5.5
30–39 Years		5.4	64.7	16.8
40–49 Years	42.5	17.8	85.7	35.0
50–59 Years	68.9	48.6	106.0	53.5
60–69 Years	191.4	115.5	139.3	75.5
79–79 Years	379.1	221.1	526.3	135.6
80 Yrs. & Over	2500.0	287.0	714.1	156.2

tion was not possible since the former represented the most severe myasthenic cases and included a large number of group III and IV patients, as well as a higher percentage of cases of thymomatous myasthenia gravis (34%), as compared to the nonoperated group (7%). Comparison between similar clinical groups of the two populations has been presented elsewhere (2).

Results

Unequivocal germinal center formation (present, frequent, numerous) was present in 33% of the men and 59% of the women undergoing thymectomy. Numerous germinal centers occurred predominately in young myasthenic women (Table I), and in women in group III (Fig. 1).

One hundred and seventy-eight deaths were attributed to myasthenia gravis. Mortality from the disease was 15% in women and 13% in men. The corresponding figures for patients with nonthymomatous myasthenia gravis were 11% and 8% respectively. Of the 39 myasthenic deaths in the thymectomy group (Table II), 56% occurred in patients with thymomas.

The majority of myasthenic deaths and one-third of the neoplastic deaths occurred within three years from the onset of the disease, while other nonmyasthenic deaths were more evenly distributed in time (Table III).

The percentage of myasthenic deaths that occurred within the first three years of the disease varied according to sex and age, and was higher in myasthenic women (61%) than in men (52%). Younger age groups had a higher percentage; in women up to the age of 40 it was 77%, while in men 58%. Similar differences were noted in the thymomatous patients.

Direct comparison of mortality in the thymomatous and the nonthymomatous myasthenic patients was not possible since most of the former underwent thymectomy, which results in a prolonged survival.

The sex and age-specific incidence of neoplasms that occurred in the 1243 patients after the onset of myasthenia gravis and prior to thymectomy was determined (Table IV). Increased incidence was found in all age groups (except in younger men) and particularly in the third and fourth decade where three-fold increase and over was noted. Myasthenic women in general had a higher incidence than men: Thirty-nine neoplasms were found in females and 25 in males, while the expected numbers in the age-matched controls were 14 and 14 respectively.

Twenty-eight myasthenic patients died from extrathymic neoplasms. Neoplastic deaths occurred only in patients who had not undergone thymectomy.

The ratio of deaths from extrathymic neoplasms to all non-myasthenic deaths was high, particularly among those deaths that occurred within three years from the onset of the disease (Table III).

Discussion

The prognostic significance of germinal centers in myasthenic patients who undergo thymectomy has been demonstrated (2, 12). Patients who have absent or rare germinal centers reach remission after a shorter interval following thymectomy compared to those with many germinal centers (2, 12). Among the myasthenic mortalities the shortest survivals were associated with numerous germinal centers and no myasthenic deaths occurred in patients with absent germinal centers (2).

In NZB mice where these thymic lesions occur spontaneously, they appear earlier in females than in males, and their incidence increases with advancing age in both sexes (4). Germinal centers are viewed by Burnet as manifestations of active proliferation of forbidden clones of immunocompetent cells (4). Transplantation of a thymus graft from infant NZB mice, in 6 to 8 month-old recipients resulted in the appearance of typical germinal centers in the graft, presumably as a result of colonization by anomalous cells present in the recipient (4).

Several similarities are noted in the distribution of germinal centers in myasthenic patients and the corresponding thymic lesions in NZB mice. Both in humans and in mice the lesions occurred more frequently in females than in males, and their degree of activity was also more prominent among the former. If these are indeed centers of proliferation of abnormal self-reacting clones of immunocompetent lymphocytes that cause autoimmune manifestations, their earlier appearance and predominance in females is noteworthy. Myasthenia gravis, a disease believed to be of autoimmune nature, is more common in women; the male to female ratio is 1:1.5. The onset and peak incidence is earlier in women (1) and the mortality from the disease among patients who do not undergo thymectomy is also higher in women (13).

A detailed study of germinal center formation in age groups was not possible since the number of specimens examined in men over the age of 30 and in women over 40 were few. Besides, in such a study, germinal center formation in residual thymic tissue from patients with thymomatous myastenia gravis should be assessed since thymomas are considered to represent the late stage in a process of which the earlier manifestations are hyperplasia and germinal center formation (14).

Clinical Course and Prognosis According to Sex

Generalized myasthenia gravis appears to be more common in females while the opposite is true of the milder ocular form of the disease (15). More than 90% of the patients who underwent thymectomy for non-thymomatous myasthenia gravis at Mount Sinai Hospital were in clinical groups IIB, III, and IV and, therefore, information on germinal centers was limited to these groups. Germinal centers were more common and more prominent in females (Table I) and the highest germinal center activity was noted in young women and in women in group III. In our series young myasthenic women and patients in group III had the highest mortality from myasthenia gravis regardless of whether they had thymectomy, but also had the highest percentage of remissions (50%) at the seventh postoperative year (2). It would seem from the present analysis, that a common characteristic in the group that presents the above pattern (poor prognosis without thymectomy and maximum benefit following thymectomy) is the presence of many thymic germinal centers. Simpson has pointed out that myasthenic deaths occur in a group whose characteristics are substantially similar to those of the group deriving most benefit from thymectomy and noted that the greater benefit obtained from the operation in women, is due to the change from a prognosis poorer than the male to one better than the male (13).

It should be stressed that patients with absent or rare germinal centers have a much better prognosis in terms of remission, interval between thymectomy and time of onset of remission, and mortality from the disease, and that the benefit obtained from thymectomy in patients with many germinal centers is relative to the poor prognosis they have without thymectomy.

Extrathymic neoplasms occur frequently in myasthenic patients (8). Increased incidence was noted both in the thymomatous and the nonthymomatous patients; they were more common in women, and their highest incidence occurred in the period after the onset of myasthenia gravis (Table IV). This most interesting trend requires confirmation in larger series. The resemblance of the incidence and mortality patterns of myasthenia gravis and extrathymic neoplasms and the frequency of the latter in sex and age groups with a high degree of activity of thymic germinal centers is consistent with the hypothesis that the allogeneic behavior of the self-reacting clones of lymphocytes may have an oncogenic potential (8).

The effects of thymectomy in myasthenia gravis have been attributed to the elimination of the centers of proliferation of abnormal clones of immunocompetent lymphocytes (2). The lifespan of thymic-derived lymphocytes is considered to be very long (16), and persistence of a pool of long-lived immunocompetent cells may be responsible for the delay in the onset of remission after thymectomy. It is also noteworthy that all myasthenic deaths in thymectomy patients occurred within four years from the removal of the thymus and that the incidence of extrathymic neoplasms decreased to expected levels three years after thymectomy (8). Sex, age, clinical category, and duration of disease do not influence significantly the long-term prognosis in the thymectomy patients; they do, however, influence the delay of the onset of remission.

Studies on the effects of neonatal (17) and adult thymectomy (18) in experimental animals have demonstrated the importance of the thymus gland in the development of immunologic competence and in immunosurveillance (19). A population of myasthenic patients offers a unique opportunity for studies of the thymic role in humans.

Thymectomy in experimental animals decreased the incidence of several neoplasms and particularly of breast carcinoma (20). Could a similar result follow the removal of the thymus gland in humans? A study of thymic role in breast carcinoma in myasthenic patients is in progress.

The physiology of the thymus in humans remains essentially unknown. The recent expansion in knowledge of the effect of thymectomy has given some answers but raised many more questions. Comprehensive and prospective studies are needed to clarify the role of the thymus in immunologic mechanisms and in human oncogenesis.

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Psychiatric Aspects of the Management of the Myasthenic Patient

ROBERT D. MARTIN, M.D. AND WALTER V. FLEGENHEIMER, M.D.

There is a slowly accumulating body of knowlege which indicates that emotions have a significant role to play in the course of myasthenia gravis. It has been noted that an emotional crisis often precedes the onset of myasthenia (1, 2); that weakness and other signs of muscular dysfunction may follow emotionally disturbing events (3); and at least one study suggested that an increased morbidity may occur in those myasthenics who have had severe emotional disorders (4). However, the psychiatric aspects of the overall management of the myasthenic has heretofore been omitted from the literature. It is for this purpose that this paper has been written.

There is no single myasthenic personality. Each patient must adjust to this chronic, often debilitating, disfiguring, disheartening, and life-threatening disease with the emotional resources and personality characteristics available to him. In many patients, psychological, physical, or social turmoil threaten the stability of the disease. It is to the advantage of the concerned physician to acquaint himself with those psychological factors which may directly affect his patient.

The authors summarize in this paper their five years' experience as members of the Psychiatry Liasion Staff attached to the Myasthenia Gravis Service at The Mount Sinai Hospital. It is hoped that this material will prove a profitable addition to knowledge acquired elsewhere.

The Newly Diagnosed Myasthenic Patient

Surprisingly, the patient who has just discovered he has myasthenia often accepts his new diagnosis with a feeling of relief. This is because he has often been through the offices of many puzzled physicians, and he finds the certainty and assurance of the staff in the myasthenia clinic to be comforting. Also remarkable is the apparent absence of depression or worry in most of these patients. With a firm diagnosis, and the calm, confident, and optimistic attitude of the treating physician, they view their disease as a problem which can be dealt with using drugs, ACTH, or thymectomy. Unfortunately, this initial impression the patient gives can be misleading and cause one to assume, incorrectly, that there are no emotional problems present or that they will not develop. Caution is preferred to this premature conclusion, and it is best to observe the patient's emotional status over a period of time before rejecting the presence of psychological problems.

In this regard it is important, at the beginning of treatment, to assess the patient's personality. How the patient handles the often severe muscle weakness

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From the Department of Psychiatry, Mount Sinai School of Medicine of The City University of New York, N.Y. 10029.

of myasthenia depends largely on his personality or character structure (5). For example, patients who have an unusual need to be cared for will accept the limitations of their illness all too readily. Consequently, they may have to be pushed so that they will not psychologically incapacitate themselves by using myasthenia as an excuse for excessive dependency relationships. Though they may be viewed as "good patients" during the acute phase of their illness, their rehabilitation during remissions or their discharge from the hospital upon recovery may be made difficult by their dependency needs.

In contrast, those who have a personality in which there is a need to defend against feelings of weakness or helplessness, will have great difficulty in accepting the limitations of their illness (1). They tend to overwork, be inconsistent in taking their medication, fail to report worsening of their condition, and tend to underestimate muscle weakness. Thus it is clear that the management of both these types of patients must be determined by their personalities as well as by the disease itself.

The Influence of Emotion on the Myasthenic Patient

MacKenzie et al and Grob (2, 6) report cases of myasthenia gravis in patients who describe distinct psychic stress occurring at the time of the onset of the disease. This association has also been observed by the authors. In two dramatic cases, the death of a family member immediately preceded the first symptoms of myasthenia. Despite the acknowledged presence of this relationship in many clinical instances, to date no controlled study has been performed in which psychic stress and its contribution to the onset of myasthenia gravis has been established. Nevertheless, the impression persists that emotional stress may be related to the onset of the disease in some cases.

Emotion affects this disease in yet another way. Once the patient develops myasthenia, emotional disturbances can exacerbate the condition. The increased weakness may be related to such diverse problems of living as marital turmoil, parental rejection, business losses, and neurotic conflicts.

Many patients report that when they become angry their condition worsens. In an attempt to prevent themselves from becoming weaker, they try to refrain consciously from the expression of these emotions. The usual psychiatric approach to these patients has to do with helping them to find ways of handling their anger by releasing it slowly, by using sublimation, or by helping them to eliminate the recurrent circumstances which create the problematic emotion. This orientation would prove inappropriate in another kind of patient who also may suffer from an emotional exacerbation of muscle weakness—the patient who denies or represses a conflict in such a way that the feelings associated with it become unconscious. Here, the unconscious complex causes difficulties in the clinical course of the myasthenic. With this type of patient the conflict must first be brought into consciousness. This can often be done through careful, detailed history-taking, paying particular attention to events preceding the exacerbation. At times, however, intensive psychotherapy is needed before the patient can deal with his conflicts in a manner that does not interfere with the myasthenia.

Heretofore, only unpleasant feelings such as rage, anxiety and depression have been discussed when describing how emotions increase muscle weakness. In our experience, some patients report that even when they feel happiness their muscle strength decreases. One twenty-one-year-old Puerto-Rican girl described the increased muscle disability when her fiance proposed marriage. This finding in a number of patients has suggested the hypothesis that the *intensity* of an emotional experience may be a significant linkage between emotion and the ensuing muscle weakness. Hence, any psychological state producing feelings above a certain threshold may be responsible for the weakness. This has suggested to us, the possibility of a hypothalamic mediating process being physiologically involved in this phenomenon.

It must be noted that some patients go through stressful psychological experiences without alteration of their myasthenia. One woman had repeated difficulties with an alcoholic husband including beatings, child abuse, abandonment, his psychiatric hospitalization and release. None of these events affected her myasthenia. On the other hand during this same time, another woman was hospitalized four times with exacerbations of weakness leading to severe respiratory problems, each following a relatively minor quarrel with a family member. Each patient reacts in his own particular manner in accordance with his unique personality. It should be kept in mind that myasthenia can be a severe, life-threatening disease. It presents a direct threat to the patient's emotional well being, and causes psychological disturbances strictly on this basis. Careful evaluation of the patient will allow one to separate the situation where emotions worsen the myasthenia from those where myasthenia worsens the emotional condition.

The Management of the Chronic Myasthenic

Depression remains the outstanding area of concern in the patient with myasthenia gravis. In the chronic myasthenic patient it is most intense when anticipated improvement from treatment is not achieved, or when he observes that his condition is worsening. This depression rarely reaches psychotic proportions. It is more like that of the neurotic variety, without the vegetative signs characteristic of the endogenous type.

In the severe myasthenic confined to bed for weeks, some depression is to be expected. These patients respond unexpectedly well to reassurance. Since myasthenia is unpredictable, even the most severely ill patient can and often does improve. This allows the concerned physician to emphasize honestly to the patient that a remission may occur, thereby boosting the patient's spirits during his difficult periods.

With the depressions which these myasthenics experience, antidepressants, though occasionally helpful, have not produced an impressive record of relief. Perhaps this is because the depression and anxiety common to these patients is so realistically based, is reactive in nature, and is not the result of some underlying psychopathology. This is supported by the repeated observation that as the patient's strength returns, his depression lifts. It is on this basis that supportive psychotherapy is viewed to be more indicated in these cases than the tricyclic antidepressants.

The importance of an open line of communication to the physician cannot be emphasized enough. Since the hospitalized myasthenic is often unable to speak, following the patient's written communications has been essential. In some instances, it has been necessary to spend a considerable amount of time trying to comprehend the patient's arduously expressed needs. Since the physician is often the only person to whom the realistically based anxieties of the myasthenic can be expressed, the time spent in this exchange is usually well worthwhile. Patients who fear dying from a faulty respirator or from pneumonia, or have some other anxiety can only be relieved when the reassuring physician has a grasp of these matters.

Management during Adrenocorticotrophic Hormone (ACTH) Treatment

The experience of the authors is that severe depression and psychosis resulting from short-term ACTH administration to the myasthenic does not occur. The occasional lift in mood which these patients experience does not present itself as a clinical problem requiring psychiatric intervention. Out of 150 courses in which ACTH was administered, only four cases of psychosis were noted. Three of these were in elderly patients in whom there was evidence that anoxia was a contributing factor. This is consistent with Alexander's study of high-dosage ACTH in the treatment of multiple sclerosis (7). In his patient population there was no psychosis observed with ACTH during 8 days of treatment and only a few cases before the end of 10 days. Only after 21 to 60 days of ACTH therapy, was a 16 percent incidence of psychosis noted.

Though a pretreatment psychiatric evaluation is performed, and though the patients are observed during the course for any mental changes, most patients do very well. Special attention is given to patients with extensive psychopathology to help them cope with the rigorous treatment. If indicated, treatment may be postponed until some confidence in the patient's emotional condition is obtained. A decision is then made either to begin therapy, watching for a worsening of the mental state, or to use other treatment modalities instead. Each case has to be evaluated separately. At present, there are no guidelines which can be used, though one factor of importance is to have the patient make a conscious and informed commitment to undertake the course of treatment.

When dealing with the patient about to receive ACTH, a number of things can be done to prevent later problems. Because it is easier for people to endure a stress with a scheduled ending, it is important to emphasize the limited, circumscribed time of the treatment. Counting the days is suggested, and this is encouraged by marking a calendar which is conspicuously posted. All of the patients are informed clearly of the extreme weakness they may experience while on ACTH. Many undergoing the treatment for the first time underestimate the degree of incapacitation and immobility which can occur. It is often useful to have the patient speak with someone who either is undergoing or has undergone ACTH treatment.

A topic which can hardly be omitted is the fact that the patient will be totally dependent on nurses and respirator. If the relationship between nurse and patient is not good, a great deal of difficulty with the patient's physical condition and well-being may ensue. Patients often are afraid to communicate their complaints about nurses, as they feel that their "life is in others' hands" and fear retaliation were they to express their anger. It is rarely possible to obtain ideal round-the-clock nursing care. One must be aware of this possible pitfall and present it for discussion with patients when the occasion arises.

Thymectomy

Thymectomy in the myasthenic presents a special problem. Before the introduction of the transcervical approach to thymectomy, the postoperative course was often stormy. It was marked by extreme weakness and psychological morbidity. Though even now an occasional patient will become depressed following the operation and there may be an exacerbation of the myasthenic symptoms, this is not a frequent problem. Problems do arise from the inability of the patient to view the procedure in a realistic manner. Most surgery is done with some immediate relief in sight. Thymectomy may give relief at once, within months, or as is often the case, within years, or not given relief at all. It is remarkable how few patients assimilate this knowledge when the physician states it frankly. To illustrate this, two examples may be given. In one case, the patient wanted immediate recovery so that she could marry her fiancé. In another, the patient was a surgeon who intensely wished to return to operating soon after his thymectomy. In these patients, the wish for immediate recovery interfered with their ability to accept the facts presented to them.

The matter of the patient's expectations from this operation must be dealt with explicitly. Where possible, the underlying emotional factors which gave rise to the need for a quick recovery should be explored and brought into awareness. The realities of this procedure must be clearly impressed on the thymectomy candidate.

The Myasthenic Patient's Family

This disease not only debilitates the individual; it also debilitates the family. Myasthenia in a husband frequently diminishes his ability to earn a living. The tendency is for him to become more dependent and less able to fulfill his role as the man of the family. His wife and children come to view him in a new perspective which demands important adaptations on their parts. His inability to earn a living poses a serious threat to the family's economic well-being. If strength and masculinity are equated by him, his behavior may become unpleasant as a result of his need to compensate. His relationship with his children may deteriorate. He may find his dependent position in the sexual act threatening. A family responding poorly to the patient because of such problems can add to his stress and worsen his condition.

The inability of a wife who has myasthenia to perform her maternal and household duties presents a great burden to family members. Unsympathetic husbands, grandparents, in-laws unwilling to help, and the presence of very young children can create stresses which worsen her condition.

The family of the myasthenic may find itself critical and suspicious of the patient and his unpredictable clinical fluctuations. This suspiciousness is especially intense where trusting relationships were not previously established. It is apparent that attention to the family of these patients is most important. Missing this area of influence may make the management of the patient more difficult. Families need to be instructed on the expectations which are reasonable for the patient. Social service assistance or psychiatric treatment may be offered when indicated. In one instance in which two teen-age brothers had myasthenia, the boys' mother had remarried after their father had died accidentally. The stepfather could not accept the "weakness" of his acquired sons. He insisted they work in the yard at heavy chores. He was physically and verbally abusive when the boys did not perform up to par. The mother's fear of her new husband caused her to abandon her sons' cause, leaving them entirely at the mercy of the stepfather. Though the myasthenia was relatively mild and the patients were able to maintain themselves in this environment, it was not without the development of psychiatric symptoms. The sixteen-year-old boy was a significantly depressed teenager when seen in the myasthenia clinic. His thirteen-year-old brother adjusted by acquiring a schizoid life style. Both needed psychotherapy.

Finally, it should be realized that the cost of medical care for the chronic myasthenic can be a severe burden. Even with extensive insurance coverage, the family may encounter financial difficulties which add to the emotional stress of the patient and his family.

Psychotropic Drugs

Phenothiazines and Antidepressants

Chlorpromazine intensifies the effects of d-tubocurarine and gallamine. Osserman, Genkins, and Kornfeld (8) state that " . . . great care should be exercised in the selection and administration of these compounds to myasthenic subjects." Practice has shown that these agents can be used safely in many myasthenics. Chlorpromazine has been used in dosages over 800 mg with no noticeable clinical neuromuscular change in the condition of the myasthenic. Imipramine and amitriptyline have also been used in dosage over 200 mg a day with no untoward results, though care should be used in adjusting the dosage. These drugs have been used without untoward results in patients receiving ACTH.

Anti-Parkinson Agents

Experience has shown that benztropine (Cogentin®) and trihexyphenidyl (Artane®) can be used to control the side effects of the phenothiazines without disturbing the medical management of the myasthenic. However, it is recommended that the patient be observed carefully so that the drugs may be discontinued should any deleterious change in the clinical condition occur.

Stimulants

It should be kept in mind that ephedrine sulfate is used as an adjuvant in the treatment of myasthenia gravis. The amphetamines and other catecholamines are considered to act similarly and may affect the therapeutic dosage of anticholinesterase drugs being administered. These stimulants have not been used by the authors. They should be used cautiously, if felt to be necessary.

Minor Tranquilizers

Meprobamate is known to " . . . depress transmission of the nerve impulse in the spinal cord and thereby cause further deterioration of muscle function . . ." (8). This and other tranquilizers (diazepam and chloridazepoxide) are known to increase muscle relaxation. Nevertheless, they have proven to cause no problem in the management of the myasthenic. All of them have been used in their usual dosage range without encountering any problems.

Sedatives

"Pentobarbital sodium (Nembutal®), secobarbital sodium (Seconal®), and phenobarbital sodium (Luminal®) increase neuromuscular blocking action of d-tubocurarine. It is, therefore, conceivable that large doses of barbiturates may have an adverse effect on neuromuscular transmission in myasthenia gravis."(8) These drugs have been used in their usual dosages in myasthenics without difficulties.

Electroconvulsive Treatment

This therapeutic modality has been used in myasthenics. Succinylcholine is, of course, avoided. In one mild myasthenic who had orthopedic and neurologic problems in addition to her psychiatric and myasthenic conditions, succinylcholine was used after much deliberation. An anesthesiologist was present and alerted to the situation. This patient had six electroshock treatments without difficulty.

Summary

This report has presented some psychiatric issues in the management of the patient with myasthenia gravis. The role of the treating physician was emphasized. The interaction of psychological factors and muscle weakness was discussed. The chronic myasthenic has difficult adjustments to make, and an awareness of the psychological factors is necessary during ACTH treatment or thymectomy, or when considering returning the patient to his family environment. The experience of the authors in the use of psychotropic drugs and electroconvulsive treatment of the myasthenic was presented.

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Contributions of The Mount Sinai Hospital to the Study and Care of Patients with Myasthenia Gravis

SOLOMON A. BERSON, M.D.

Major advances in the understanding and treatment of myasthenia gravis have been few and far between. Almost two score years were to elapse before Mary Walker in 1934 (1) acted on Jolly's earlier suggestion that physostigmine was worthy of therapeutic trial in myasthenia on the basis of the similarity of the symptoms of the disease to those of curare poisoning (2). Five years afterwards Blalock showed that thymectomy was beneficial to some patients with the disorder (3), but not until 30 years later was there introduced a far less traumatic procedure in the rediscovery of transcervical thymectomy (4). Therapy with ACTH was abandoned shortly after its introduction in 1948 (5) because of frequent exacerbations of symptoms and often fatal respiratory depression. Not until almost two decades later did advances in acute respiratory care permit the safe reinstitution of what was originally regarded as a form of "medical thymectomy" (6).

Neither the etiology nor even the basic physiologic defect in myasthenia gravis has been satisfactorily elucidated. The response to thymectomy or ACTH is not understood and the role of autoimmunity is still being investigated without clear-cut conviction of the primacy of an underlying immune process. Yet in spite of the abysmal bewilderment as to the nature of this disorder, and whether, indeed, the nervous system, the muscle membrane, or the lymphocyte (or its relatives) is to be indicted, the care and even the cure of patients with myasthenia gravis have progressed. No small part of therapeutic success is to be credited to those few physicians who have invested their careers in the study of the disease. In the assiduous attention given to every threatening complication and in the constant vigilance against the hazards of respiratory infection and the various crises that are part of the way of life of the severely afflicted myasthenic patient, few other diseases have demanded from these physicians such dedicated effort extended over such long periods.

Dr. Kermit E. Osserman and his colleagues in The Mount Sinai Myasthenia Gravis Clinic are to be hailed as members of that small cadre of physicians who have contributed immensely to diagnosis and treatment of the disease, who have provided a firm basis for evaluation of the benefits of various therapeutic procedures, and who have continued to engage in the forefront of basic and clinical investigations on the pathologic physiology of myasthenia gravis. The papers in this issue of the Journal review current knowledge of myasthenia gravis and summarize the experience of the Mount Sinai group, occasionally in collaboration with other large clinics, in the long-term care of over 1000 patients with the disease. Some of the studies of the Mount Sinai group are

Murray M. Rosenberg Professor and Chairman of Medicine, Mount Sinai School of Medicine of The City University of New York, N.Y. 10029; Director of Medicine, The Mount Sinai Hospital, New York, N.Y. 10029.

described in detail in the preceding articles. The contributions of these workers are perhaps most succinctly summarized in the appended annotated bibliography. Particularly noteworthy in the clinical area are the introduction of the edrophonium test for the rapid diagnosis of myasthenia gravis (1, 2 in the annotated bibliography) and later for the differentiation between cholinergic and myasthenic crises (3–5 annotated bibliography), improvement in the management of patients undergoing thymectomy by performance of tracheostomy, and attention to tracheobronchial toilette (16, 17 annotated bibliography), rediscovery of the transcervical approach to total thymectomy (27 annotated bibliography), and, in collaboration with the Maimonides Hospital group, a thorough evaluation of massive ACTH therapy (30 annotated bibliography). Also, the Mount Sinai group, alone or in collaboration with workers in other institutions, has undertaken significant investigations on the immune aspects of myasthenia gravis (51–66 annotated bibliography).

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